Guidelines for noninvasive ventilation in acute respiratory failure

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Non-invasive ventilation (NIV) refers to the application of artificial ventilation without any conduit access to the airways i.e., without an endotracheal or tracheostomy tube. NIV has now assumed a prominent role in the management of acute respiratory failure[1-6] Possible indications of NIV has increased both in and out of hospital settings. By avoiding endotracheal intubation, NIV decreases incidence of complications associated with invasive ventilation like airway problems, nosocomial pneumonia (21%) and sinusitis (5-25%).[7-10]

The purpose of this document is…

- To disseminate updated information regarding the appropriate use of NIV by the physicians involved in the care of critically ill patients in India.
- To provide guidelines for appropriate application of NIV in acute respiratory failure.
- To give guidelines for selection of interface, mode of ventilation, choice and use of ventilators and their maintenance.
- To set the minimum standards for care of patients receiving NIV in and outside ICU.
- To provide guidelines for setting up an NIV facility.
- To promote research on this subject in the country.

Methods

The executive committee of Indian Society of Critical Care Medicine selected the chairperson. The chairperson then identified the members of the committee from amongst prominent workers in the field from all over India. Each member was allotted one aspect of the guidelines. All the members prepared the allotted aspect.

All these sections were presented and discussed in a meeting and modifications were suggested. The chairperson then compiled all the sections into one draft document, which was sent to all the members. This was followed by a series of meetings where each recommendation was discussed and graded. The first guidelines were published in 2006.

The executive committee of Indian Society of Critical Care Medicine decided to revise the existing guidelines. Chairperson with the help of members prepared a revised document after an intensive literature search, which included Medline, Cochrane analysis and references in major articles from 1980 to 2012.

The current guidelines were sent to all the participants and they were asked to update the section allotted to them last time. Then document was discussed among the members for their views. The changes suggested by the members were then incorporated by the chairman.

The guidelines were than circulated among members for final comment. This final statement represents the result of this process.

Grading of recommendations

Wherever applicable, recommendations were graded on the basis of modified version of the evidence-based recommendations, which have been used earlier for grading for community-acquired pneumonia.[12] All available and relevant articles till Dec 2012 were considered. Evidence based recommendations were chosen as they are dynamic and they can change as new evidence becomes available.

Evidence based grading system used to rank recommendations

Evidence level	Definition
Level I (High)	Evidence comes from well-conducted, randomized controlled trials

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Level II (Moderate)	Evidence comes from well-designed, controlled trials without randomization (including cohort, patient series and case control studies). Level II studies also include any large case series in which systemic analysis of NIV use was conducted
Level III (Low)	Evidence comes from case studies and expert opinion

Indications

There are a large numbers of studies describing the use of NIV in various conditions but most of the randomized controlled trials (RCT) have been done predominantly in COPD. Evidence is accumulating on the use of NIV in other conditions.

There are four ways in which noninvasive mechanical ventilation can be used[1,2,5]

- Noninvasive mechanical ventilation can be used in addition to medical treatment in selected patients of respiratory failure early in the course of illness as a measure to avoid tracheal intubation
- When invasive ventilation is indicated, a trial of NIV can be given before intubation in selected patients
- Noninvasive mechanical ventilation can be used in patients who are not candidates for intubation or in patients who refuse intubation
- Noninvasive ventilation can also be used during weaning from invasive ventilation to avoid reintubation.

Hypercapnic respiratory failure

Chronic obstructive pulmonary disease

Patients with COPD are prone to exacerbations with progression of their disease. A significant number of COPD exacerbations are complicated by hypercapnic respiratory failure with significantly increased mortality and morbidity. Tracheal intubation and mechanical ventilation has so far been the standard modality for managing these patients; which is associated with significant complications.

In the last decade many studies have been published on the role of NIV in treating severe episodes of acute respiratory failure in COPD patients. This has dramatically modified outcome in these patients.[13-31] These well-conducted, randomized controlled trials have shown that when NIV is used in addition to standard medical therapy, it decreases rate of endotracheal intubation rate and mortality as compared to medical therapy alone.[13-23] The majority of these studies included patients with severe exacerbation of COPD who had pH <7.35 and higher intubation rates in their control groups. There are only few studies, which have not shown any benefit of NIV. These studies tended to include patients with mild respiratory failure.[24,25] NIV also shortens the length of ICU and hospital stay compared with medical therapy alone.[14,15] Several meta-analyses have been published on these controlled trials.[28-29]. Lightowler *et al.* in a Cochrane review have shown that the application of NIV in patients with hypercapnic respiratory failure is advantageous in terms of decreasing intubation rates, treatment failure and mortality and it should be applied early, before severe hypercapnia and acidosis ensue.[28] Keenan *et al.* systematically analyzed the results of 15 studies and came to the same conclusions.[29] In addition, they also found that the benefits of NIV were not demonstrated in patients with mild exacerbation.

Most of the above mentioned studies excluded patients who required immediate intubation. However, another RCT reported use of NIV versus conventional mechanical ventilation in patients who had a mean pH of 7.2 and who failed medical treatment and required immediate assisted ventilation[21] In these patients, noninvasive ventilation was no worse than endotracheal intubation.[21] The intubation rate in NIV group was 52%, which is higher than in other randomized controlled trials, which is not surprising because sicker patients who had failed medical treatment were included in the study. This trial illustrated that even at this stage, intubation was avoided by NIV in almost 50% patients but there was no significant difference in ICU or hospital mortality.[21,32] The patients who could be managed by noninvasive ventilation successfully required less hospital admission in the year after hospital discharge.

Squadrone *et al.*[22] evaluated the effects of NIV in patients with COPD who were deemed to require intubation and compared the outcome with a matched set of patients who had earlier been ventilated invasively for COPD. Though 40 out of the 64 patients on NIV needed intubation, the mortality rate, duration of invasive ventilation, length of ICU and post ICU stay were not different between the two groups. Compared to those who needed intubation, patients who were successfully managed with NIV had decreased mortality rate and length of ICU and post ICU stay.

In another RCT, it has been shown that hypercapnic coma with GCS <8 can be treated as successfully as awake patients with NIV.[23] In this open non-controlled study, between groups of acute respiratory failure patients with GCS scores less than 8 vs. more than 8, the mortality rates were similar. Thus, the beneficial effects of NIV are also seen in the sicker sub group of COPD patients. One must remember, however, that these studies were conducted in the controlled environment of an ICU where facilities for close monitoring were available.

In the review by Keenan *et al.*[33], 14 out of 16 identified RCTs had lower incidence of endotracheal intubation (RR 0.39, 95% confidence interval [CI] 0.28-0.54) and hospital mortality (RR 0.52, 95% CI 0.36-0.76) among patients who received noninvasive positive-pressure ventilation. Most of these trials included patients with severe exacerbations with arterial pH <7.35. 3 RCTs which included patients with milder exacerbations did not showed reduction in risk of endotracheal intubation (RR 0.71, 95% CI 0.16-3.08) or hospital mortality (RR 1.05, 95% CI 0.07-6.36).[33]

Celikel *et al.*[20] have also shown that early NIV had a success rate of 93% whereas the same was reduced to 67% if initiated late.

RCTs by Antonelli *et al.*[34] and Li *et al.*[35], compared noninvasive positive-pressure ventilation with intubation and conventional mechanical ventilation for patients with severe exacerbation of COPD requiring immediate assisted ventilation. Use of noninvasive positive-pressure ventilation resulted in avoidance of intubation in more than half of the patients, but there was no significant difference in the intensive care unit or in hospital mortality. In a randomized controlled crossover trial, Dreher *et al.*[36] compared the 6 weeks of high intensity NIV (mean inspiratory pressures of 28.6 ± 1.9 mbar) with low intensity NIV (mean inspiratory pressures of 14.6 ± 0.8 mbar) in controlling nocturnal hypoventilation in patients with severe chronic hypercapnic COPD. High intensity NIV was better tolerated and shown to be superior in controlling nocturnal hypoventilation. Jolliet P[37] evaluated the use of helium–oxygen (heliox; 80:20 mixture) in addition to NIV for patients with exacerbation of COPD.and found, no difference in rate of endotracheal intubation (8/59 with heliox versus 13/64 for control; $P = 0.33$) or hospital mortality (9/59 v. 6/64; $P = 0.48$). A multicentre prospective RCT by Maggiore *et al*.[38] did not show statistical superiority of using helium during NIV to decrease intubation rate during acute exacerbation of COPD.

All these studies conclude that when applied in addition to standard medical therapy in COPD patient with acute hypercapnic respiratory failure, NIV results in the following:

- Reduction in the rate of endotracheal intubation
- Reduction in the in-hospital mortality
- Reduction in the complications like nosocomial pneumonia
- Reduction in ICU and hospital length of stay.

Recommendations

- NIV should be considered in patients of COPD in addition to standard medical therapy, when they present in acute severe exacerbation (pH <7.35, and hypercarbia). (Level 1)
- Patients with relatively mild exacerbation of COPD (pH >7.35) may not benefit from NIV. (Level II)
- NIV can be administered both in ICU as well as in general medical/emergency wards in COPD patients, though patients with a relatively severe exacerbation (pH <7.30) are better managed in an ICU setting. (Level II)
- No recommendation can be made currently about the use of NIV versus intubation and conventional mechanical ventilation in patients who have a severe exacerbation of COPD that requires assisted ventilation, because of insufficient evidence
- Heliox cannot be recommended routinely in patients with severe exacerbation of COPD who are receiving NIV. (Level II)

Practice points

- At the time of presentation, all patients with acute exacerbation of COPD should have arterial blood gas analysis besides clinical evaluation
- NIV should be started in ICU. However, in less severe cases, a trained nurse or respiratory therapist can administer it in medical wards or in the emergency room
- The important point is to initiate it as early as possible. Patients on NIV should be closely monitored during the first 1-2 hours and ABG should be repeated, at the end of 1 and 4 hours
- For the first 24 hours NIV should be given for as much time as possible except during feeding and physiotherapy. Later on, the duration can be decreased depending upon the clinical condition and physiological parameters (SpO_2 and ABG).

Neuromuscular disease/chest wall deformity

NIV is effective in chronic ventilatory failure due to chest wall deformity and neuromuscular diseases. However, there are very few studies, which have examined the use of NIV when these patients become acutely ill. These patients constitute a very small proportion of patients with respiratory failure[39-41] There are no randomized controlled trials but only a few retrospective case series, which have suggested that NIV alleviates gas exchange abnormalities and avoids intubation in patients with neuromuscular diseases and kyphoscoliosis who present with respiratory failure.[41]

Recommendations

NIV may be tried in patients with neuromuscular disease and chest wall deformity when they present in acute -on-chronic respiratory failure. (Level III)

Acute asthma

One may assume that NIV should be as effective in asthma as in COPD, both being disorders of airway resistance. However, this has not been confirmed by any randomized controlled trials. This may be due to the fact that the natural history and pathophysiology of asthma is entirely different.[42-46]

In a retrospective analysis of 33 asthmatics, the outcome of 22 patients managed with NIV was compared with 11 patients who were managed by endotracheal intubation and ventilation. NIV patients were less hypercapnic and gases improved rapidly in this group.[42] In a randomized controlled trial, Soroksky *et al.*[44] has shown that in selected patients with severe asthma, the addition of NIV to conventional treatment can improve lung functions, alleviate exacerbation faster and reduce the need for hospitalization. However, in another randomized trial no benefit of NIV was demonstrated.[46]

In an l small RCT by Soma *et al.*, comparing two pressure levels noninvasive positive pressure ventilation with oxygen therapy alone, a greater reduction in dyspnea and a greater increase in FEV1 were reported for the NIV group.[47] Although the evidence for the use of NIV in asthma is inconclusive[45] a trial on NIV in carefully selected patients is justified, particularly in patients who fail to respond promptly to medical treatment and have no contraindication. It has also been suggested that aerosolized medicines may be delivered more effectively by NIV.[48]

In a retrospective cohort study by Murase *et al.*,[49] the need for endotracheal intubation in severe attack of asthma was decreased after introduction of NIV. They concluded that NIV is a useful and acceptable method of stabilizing patients with severe attack of asthma. In a meta-analysis by Ram *et al.* concluded that application of NIV in patients with status asthmaticus still remained controversial.[45] Large prospective randomized controlled trials are needed to determine the role of NIV in these patients.[45]

Recommendations

- NIV is not recommended for routine use of asthma exacerbation. (Level II)
- NIV may be tried in ICU in patients of acute severe asthma who fail to respond quickly to medical treatment and have no contraindication. (Level III)

Acute respiratory failure in obstructive sleep apnea

Patients with acute or chronic respiratory failure caused by severe obstructive sleep apnea syndrome have been treated successfully with NIV.[50] CPAP has also been used in these patients of severe decompensated obstructive sleep apnea.[51] If respiratory acidosis is present, NIV should be used and they should be transitioned to CPAP once they are stable. So far, there are no randomized controlled trials to prove this application. NIV therapy has also been found to be effective in the treatment of patients with obesity hypoventilation syndrome providing a significant improvement in the clinical status and gas exchange.[52] Carrillo *et al.* compared the efficacy of NIV in episodes of AHRF caused by OHS and COPD in 716 consecutive patients (173 with OHS and 543 with COPD) with AHRF (arterial pH <7.35 and Pa (CO (2)) >45 mm Hg) treated with a similar protocol of NIV. They concluded that patients with OHS can be treated with NIV during an episode of AHRF with similar efficacy and better outcomes than patients with COPD.[53]

Recommendations

- CPAP/NIV is recommended for obstructive sleep apnea presenting as acute respiratory failure. (Level III)
- NIV is recommended for patients of obesity hypoventilation syndrome (Central alveolar hypoventilation syndrome) with acute respiratory failure. (Level I)

Cystic fibrosis

There are few case series on the role of NIV in patients with cystic fibrosis. Hodson *et al.*[54] used NIV in six patients with Cystic Fibrosis who developed acute retention of CO_2 superimposed on chronic retention. Out of the six patients, four survived until heart-lung transplant. In another large study the same team[55] used NIV in 113 patients with cystic fibrosis who were being evaluated for lung transplant and experienced acute respiratory failure. Eight had successful transplant and ten were on waiting list.

NIV resulted in improvement in hypoxemia in these patients but not in hypercapnia. Flight *et al.* studied 47 patients with cystic fibrosis from 1991 to 2010, of whom 36% underwent lung transplantation, 28% died without transplantation and 30% remain alive on NIV. They concluded that NIV may slow or reverse the decline in lung function in advanced CF. NIV was increasingly used beyond a bridge to transplantation at their centre.[56]

Recommendations

- NIV may be helpful as rescue therapy to support acute respiratory failure in cystic fibrosis, providing a bridge to lung transplantation. (Level III)

Interstitial lung diseases

The evidence for use in interstitial lung disease (ILD) in terminal stage is limited although it has been mentioned in case series. In end stage of ILD, these patients have severe hypoxemia and low lung compliance. NIV would not be expected to offer much benefit.[57]

Recommendation

NIV is not recommended for interstitial lung disease with acute or chronic respiratory failure. (Level III)

Acute hypoxemic respiratory failure

Data on successful application of NIV in patients with acute hypoxemic respiratory failure is less and conflicting. This is mainly due to varied etiologies in the sub groups of patients causing hypoxemic respiratory failure (HRF) included in most of the published studies.[58-73]

The first RCT of NIV among non-COPD patients with HRF, conducted by Wysocki *et al.*,[58] found no benefit in terms of reduction of intubation rate or hospital mortality. Since then, a number of randomized controlled trials[58-62] that included patients of HRF have produced conflicting results.

The meta analysis by Wysocki *et al.* and Keenan *et al.*[61,73] of the randomized trials[58-70] suggests that patients with hypoxemic respiratory failure are less likely to require endotracheal intubation when NIV is added to standard therapy. However, the effect on mortality is less clear and the heterogeneity among studies suggests that its effectiveness varies among different patient populations. As such, suggesting that NIV is beneficial for all patients presenting with acute hypoxemia would be misleading.[73] In addition, the diagnostic category of hypoxemic respiratory failure is too broad to apply to individual patients in these studies. Recently, a few studies have focused on some of the individual diagnoses within the large category.[89-95] It has been found to be very effective in cardiogenic pulmonary edema.[66,72,74,83] NIV may also be efficient when some components or degree of cardiac decompensation participates in the clinical feature, even if it is not the main or only cause of episode of respiratory failure.

Recommendations

- NIV may be useful in selected patients of hypoxemic respiratory failure. (Level I)
- NIV can be tried in ICU in hypoxemic respiratory failure. (Level III)

Role of NIV in cardiogenic pulmonary edema

A number of randomized controlled trials[66-75], have studied the use of noninvasive ventilation in acute cardiogenic pulmonary edema. They have compared CPAP with standard medical therapy to standard medical therapy alone, NIV with standard medical therapy versus standard medical therapy alone, CPAP with standard therapy versus NIV with standard therapy alone or combinations of these 3 treatments and found similar results with the two techniques in terms of improvement in arterial blood gases, respiratory frequency and reduction in endotracheal intubation rate.

Recently, NIV has increasingly been used in combination with medical treatment for acute cardiogenic pulmonary edema.[66,72,74,83,84] Nava *et al.*,[78] in the emergency department, found that NIV improved PaO_2/FiO_2 ratio, respiratory rate and dyspnea significantly faster than the group receiving medical therapy plus oxygen. However, intubation rate, hospital mortality and duration of hospital stay were similar in the two groups. In the sub group of hypercapnic patients, NIV improved $PaCO_2$ significantly faster and reduced the rate of intubation compared with medical therapy. Adverse events, including myocardial infarction, were evenly distributed in the two groups.

In a prospective randomized controlled trial, Salman *et al.*[96] concluded that in patients with acute cardiogenic pulmonary edema, NIV results in a more rapid improvement in respiratory distress and metabolic disturbance compared to standard medical therapy but no improvement in short-term mortality. Chadda *et al.*[79] found NIV superior to CPAP in unloading the respiratory muscles when patient were studied after at least 24h stabilization period. In another study, Mehta *et al.*,[71] comparing pressure support plus PEEP with CPAP in patients with acute cardiogenic pulmonary edema showed that NIV reduced the sensation of dyspnea and improved the gas exchange more than CPAP alone but they found a higher rate of myocardial infarction in the Pressure Support group. Following this, several studies have compared NIV and CPAP directly over the past year and found both to be equally effective in the treatment of acute cardiogenic pulmonary edema.[80,81,82] In addition, these studies also indicated that NIV does not increase myocardial infarction rates.[80,82]

In a recent large RCT which compared NIV, CPAP and oxygen therapy alone, rapid improvement in respiratory distress and metabolic disturbances was found in NIV group alone but no significant effect on mortality, (84). In a meta-analysis by Weng *et al.*[97] that included randomized trials comparing continuous positive airway pressure and bilevel ventilation with standard therapy or each other, they found that evidence still supports the use of NIV in acute cardiogenic pulmonary edema. Continuous positive airway pressure reduces mortality more in cardiogenic pulmonary edema due to acute myocardial ischemia. In a recent review on NIV, lower hospital mortality (NIV; RR 0.84, 95% CI 0.63-1.13 and CPAP; RR 0.73, 95% CI 0.51-1.05) was reported in acute cardiogenic pulmonary edema.[2]

Recommendations

- CPAP/NIV is recommended in addition to standard medical treatment in cases of cardiogenic pulmonary edema. (Level I) NIV is preferable in patients associated with hypercapnic respiratory failure (Level II)
- CPAP/NIV is equally effective in cardiogenic pulmonary edema (Level I).

Role of NIV in transplant and Immunosuppressed patients

In immunosuppressed patients with acute respiratory failure invasive mechanical ventilation is associated with high mortality rate.[98] A number of studies have underlined the worst prognosis for neutropenic patients with acute respiratory failure requiring invasive mechanical ventilation.[98] NIV seems to be an alternative in these patients because of the lower risk of complications; as it prevents endotracheal intubation and its associated complications.[98]

In a randomized trial of 40 solid organ transplants patient with HRF, Antonelli *et al.*[63] compared NIV with facemask to standard treatment and found a significant reduction in rate of endotracheal intubation, fatal complications, length of stay in the ICU and ICU mortality. However, there was no difference in-hospital mortality.

In another prospective RCT, by Hilbert and colleagues,[64] 52 immuno-suppressed patients (30 patients with hematological malignancies and neutropenia, 18 who received immunosuppression to prevent rejection of solid organ transplantation and four with HIV syndrome), were randomized to receive conventional medical treatment or NIV plus conventional treatment. Patients were recruited at an early stage of HRF. NIV significantly reduced the rate of intubation and serious complications. Both ICU and hospital mortality were significantly reduced. In this prospective RCT on immunocompromised patients treated with NIV, authors obtained impressive results in the sub group of patients with hematological malignancies and neutropenia.

In another recent retrospective study involving 158 Italian ICUs, better outcome was observed in patients with successful NIV compared to invasive ventilation or invasive ventilation after NIV failure in patients with hematologic malignancies, particularly in patients with ARDS.[99]

Recommendation

NIV is recommended early in the course of hypoxic respiratory failure in immunocompromised patients, particularly in those with hematological malignancies. (Level I)

Role of NIV in lung resection surgery and abdominal surgery

Thoracic and upper abdominal surgery are associated with marked and prolonged post operative reduction in functional residual capacity, leading to hypoxemic respiratory failure due to widespread atelectasis at basal lung zones.

Auriant *et al.*[85] conducted a randomized controlled trial in patients who experienced respiratory distress after lung resection. With the use of NIV, a reduction in endotracheal intubation and a clear benefit in terms of hospital survival was observed.

The use of NIV to prevent respiratory failure who underwent high risk surgical procedure that include major vascular procedures, such as elective abdominal vascular surgery, lung resection surgery or thoracoabdominal vascular surgery had been tried in few trials.[85,202] The result from these two trials showed a reduced rate of endotracheal intubation but no significant difference in hospital mortality.

However before initiating NIV in postoperative patients with ARF, a surgical complication should be eliminated and treated. Use of postoperative NIV in high risk patients by a trained and experienced ICU team, with careful patient selection, can be considered.

Recommendation

NIV may be used in patients who develop respiratory distress or respiratory failure after lung resection or abdominal surgery. (Level II)

There is no recommendation about the use of NIV to prevent respiratory failure after high-risk surgical procedures, because of a lack of RCTs.

Role of NIV in severe community acquired pneumonia

Few studies have reported the use of NIV in patients with HRF in community acquired pneumonia (CAP) and published results are conflicting.[60,86,87], Among 30 patients with hypoxemic respiratory failure receiving NIV, Benhamou *et al*.[87] found no difference in response rate in patients with and without pneumonia.

Confalonieri *et al*.[60] demonstrated major benefit of NIV in patients with severe CAP, by reducing the rate of endotracheal intubation and duration of stay. This benefit, however, was almost entirely explained by the subgroup of patients with COPD. Other studies of severely hypoxemic patients with pneumonia have shown a high rate of failure in this sub group.[88-90] NIV cannot therefore be recommended for all patients with severe CAP.

Ferrer *et al*.[59] showed that, provided a very careful selection of the patient performed (exclusion of hemodynamic instability, several organ failures, lack of cooperation, abundant secretions etc.), NIV can be very successful in community acquired pneumonia.

Recommendation

- NIV may be used in the ICU with caution in selected patients with community-acquired pneumonia particularly in those with associated COPD (Level II)
- NIV cannot be recommended with severe community-acquired pneumonia without prior history of COPD, because of insufficient evidence.

Role of non invasive ventilation in ARDS

There is limited literature on the use of NIV in ARDS. In an uncontrolled study by Rocker and coworkers,[91] NIV was applied with the help of facemask to ten patients with ARDS. Intubation was avoided in 67% of patients. Two controlled studies[63,65] comparing NIV with a conventional approach included some patients of ARDS. The rate of intubation was 40% for patients of ARDS randomized to NIV and the mortality rate in these patients was 35%. But in a multicentre RCT involving patients with mild ARDS, NIV significantly decreased intubations but nonsignificantly decreased hospital mortality.[101] They concluded that NIV is safe in selected patients with mild ARDS.

In a prospective cohort study, in European intensive care units, NIV could avoid intubation in up to 54% of treated patients. A Simplified Acute Physiology Score (SAPS) II >34 and the inability to improve Pao_2/Fio_2 after 1 hr of NPPV were predictors of failure.[102]

Agarwal R *et al*.[104] analysed the role of non-invasive ventilation in acute lung injury/Acute respiratory distress syndrome in 13 studies. They concluded that there is risk of an almost 50% NIV failure rate in patients with ALI/ARDS. So NIV should be cautiously used in patients with ALI/ARDS. There is a need for a uniform NIV protocol for patients with ALI/ARDS.

In a study by Chen *et al*.[92] NIV resulted in improvement of vital signs, gas-exchange and sense of dyspnea and they recommended that NIV could be used as a substitute tool for endotracheal intubation in selected patients of SARS. Han *et al*.[93] reported the successful use of NIV in hypercapnic patients of SARS. Endotracheal intubation was however required in 1/3rd of the patients who initially had a favorable response to NIV.

The above results should be interpreted cautiously and one should be very careful while applying NIV in ARDS patients. It should ideally be restricted to hemodynamically stable patients who can be closely monitored and where facility for endotracheal intubation is available.

Severe H1N1 pneumonia with ARDS

With recent 2009 pandemic H1N1 with severe ARDS, use of NIV was reported by few case reports and two prospective cohort studies. They found that NIV was used in 25% to 30% of patients but had very high failure rates with 70% to 90% of these patients' required subsequent intubation and invasive ventilation. In a prospective study involving 98 patients with new pulmonary infiltrate (s) sustained by H1N1 virus and a PaO_2/FiO_2 <300. 38/98 required immediate endotracheal intubation, while the others received NIV as a first line therapy; 13/60 patients failed NIV and remaining 47/60 patients were successfully ventilated with NIV. It was concluded that early application of NIV, with the aim to avoid invasive ventilation, during the H1N1 pandemics was associated with an overall success rate of 47/98 (48%). Patients presenting at admission with high SAPS II score and a low PaO_2/FiO_2 ratio and/or unable to promptly correct gas exchange are at high risk of intubation and mortality.[94]

Recommendation

- NIV may be used with great caution in cases of Mild ARDS and that too only in controlled settings of an ICU. (Level III)
- The application should be reserved for hemodynamically stable patient who can be closely monitored in an ICU where facilities for invasive ventilation are present.

Trauma

Patients who sustain trauma can develop respiratory failure. Some of these patients with a flail chest or mild acute lung injury might respond to NIV therapy. In a retrospective analysis of 46 trauma patients who were treated with NIV, Beltrame *et al.* found rapid improvement in gas exchange and success in 72% of the patients.[95]

CPAP with regional anesthesia when compared to invasive ventilation in patients with chest trauma resulted in fewer ICU and hospital days for CPAP group.[103] In another study, when NIV along with regional anesthesia was used in patients with blunt thoracic trauma with acute respiratory failure, it proved to be a safe and effective method to improve gas exchange in these patients.[105] Another RCT, reported a lower mortality rate (2/22 v. 7/21; $P < 0.01$) for the group receiving CPAP by mask, but the small number of patients ($n = 43$) and the single-centre design raise concerns regarding general applicability of these findings. These patients should however be treated in ICU. In a single centre prospective randomized controlled trial involving severe thoracic trauma patients with PaO_2/FiO_2 ratio <200, NIV significantly reduced intubation compared to oxygen therapy.[106]

Recommendation

CPAP or NIV can beconsidered for hemodynamically stable patients of chest trauma with respiratory distress. (Level II)

Role of NIV in "do not intubate" patients for palliative care

There is a group of patients with acute respiratory failure who are poor candidates for endotracheal intubation due to advanced age or co-morbidity. There are also patients who do not want intubation (DNI) but accept NIV. Levy and colleagues[107] instituted NIV to a group of 114 patients with DNI status for ARF and found that 49 (43%) patients could be treated successfully and survived to discharge.

Patients with congestive heart failure had significantly better survival than those suffering from COPD, cancer, pneumonia or other diseases. Meduri *et al.* had shown that NIV offers an effective, comfortable and dignified method of supporting patients with end stage disease and acute respiratory failure.[11]

Recommendation

NIV can be recommended in selected do not intubate" patients. (Level II)

Role of NIV for preoxygenation

In a prospective randomized study, Baillard *et al.* compared the preoxygenation by the noninvasive ventilation and nonrebreather bag-valve mask. Preoxygenation was performed for 3 minutes before rapid sequence intubation. At the end of preoxygenation, arterial oxygenation was significantly higher and significantly lesser number of patients had arterial desaturation in the noninvasive ventilation group. They concluded that preoxygenation was better performed with noninvasive ventilation compared to nonrebreather bag-valve mask.[108]

In a prospective multicentre controlled study, Jaber *et al.* concluded that implementation of intubation management protocol can reduce immediate life threatening complications associated with endotracheal intubation in ICU patients.[109] Preoxygenation with noninvasive ventilation constituted an important part of this protocol. In another randomized controlled study including morbidly obese patients, noninvasive ventilation improves oxygenation better compared to conventional methods of preoxygenation during induction of anesthesia.[110]

Recommendation

NIV can be recommended for better preoxygenation during induction of anesthesia. (Level I)

Role of NIV during fiberoptic bronchoscopy (FOB)

Fiberoptic bronchoscopy is a usual procedure to establish the diagnosis in acute respiratory failure. But these patients are at risk of endotracheal intubation during fiberoptic bronchoscopy.[2] NIV might decrease the risk of bronchoscopy related complications in patients with hypoxemic respiratory failure.[111] In a small prospective study[100] by Agarwal *et al.*, including 6 patients with PaO_2/FiO_2 ratio <200, FOB was performed NIV support. NIV was started 10 minutes before and continued for 30 minutes after the procedure. All patients maintained SpO_2 >92% during FOB. In another prospective study by Clouzeau *et al.*, they concluded that FOB bronchoalveolar lavage can be performed safely in hypoxemic patients on NIV.[112]

In another prospective study involving 40 hypoxemic patients requiring NIV, Baumann *et al.*, concluded that FOB can be performed with an acceptable risk.[113]

Recommendations

NIV can be used in selected hypoxemic patients to perform fiberbronchoscopy. (Level III)

Practice Points for hypoxemic respiratory failure

- These patients should preferably be ventilated with a full-face mask during the acute phase and may be shifted to nasal mask once the condition stabilizes
- Hypoxemic respiratory failure should preferably be treated with an ICU ventilator as a higher Fio_2 can be administered with it
- Pressure preset modes with PEEP are recommended in these patients. The ventilator used to provide NIV should have a fast rise time and ability to increase the inspiratory flow rates to maintain constant pressure in the face of major air-leaks
- Non-invasive mechanical ventilation should be discontinued if there is (a) no improvement in gas-exchange and dyspnea (b) significant mouth leak, (c) severe mask intolerance or (d) no improvement in mental status within 30 min of the application of NIV in an agitated hypoxemic patient.[75]

NIV in weaning from mechanical ventilation

NIV can be used to reduce muscle fatigue and can thus serve as a bridge between invasive support and spontaneous breathing to reduce the time on invasive mechanical ventilation. It is attractive to speculate that the many complications of endotracheal mechanical ventilation (ETMV) can be prevented by successful early weaning to NIV. This principle can also be extended to include the postextubation period in an attempt to reduce the incidence of reintubation and the additional risks of late nosocomial pneumonia.

NIV has been applied in the following 3 ways for either reducing time on endotracheal mechanical ventilation or for preventing reintubation:

- As a part of an early weaning strategy, when patient fails a trial of spontaneous breathing
- After conventional weaning and extubation to prevent postextubation failure
- When signs of respiratory failure develop after extubation.

As a weaning strategy in patient who fails a trial of spontaneous breathing

Case series[114] and studies by Nava *et al.*[115] and Ferrer *et al.*[116] support the use of NIV in this condition for selected patients of COPD. However, most of these trials included only patients who had exacerbations of COPD. However, for the non-COPD respiratory and primarily non-respiratory conditions, evidence for its benefit is lacking.

Nava *et al.*[115] studied the efficacy of NIV for early extubation in patients of COPD on mechanical ventilation. In this 3-centre prospective study, patients were initially mechanically ventilated for 48 hours and then extubated after a successful spontaneous breathing trial (SBT). Those who failed the SBT were randomized to two groups. The intervention group was extubated to NIV support and the conventional group continued to be on MV for gradual weaning through daily reductions of pressure support. There were predetermined criteria for reintubation. When NIV was thus combined with a 48-hr period of invasive ventilation, the total period of ventilation, ICU stay, and incidence of pneumonia and 60-day mortality were reduced.

In a prospective, randomized, single center study by Girault *et al.*,[116] continued invasive pressure support was compared with systematic extubation to NIV support in patients who failed a 2-hour weaning trial. With matched baseline characteristics, the NIV group had a shorter duration of invasive ventilation but there was no reduction in the total duration of respiratory support or of 3-month mortality.

Ferrer *et al.*[117] similarly studied the efficacy of NIV in reducing the time of weaning from invasive ventilation. This multicentre Spanish study involved 43 mechanically ventilated patients who had failed weaning trials for 3 consecutive days. NIV was applied virtually continuously in the first 24 hours postextubation. This study also showed decreased mortality, ICU days and incidence of VAP, septic shock and total mechanical ventilator days in the NIV as compared to the control group. Additionally, this study also showed a reduced incidence of tracheostomy in the NIV group.

However The methodologic limitations and general applicability of these results is still under question because of concerns like safety, feasibility andresource limitations, hence the use of NIV for these patients requires both considerable expertise and the ability to closely monitor the patients, because urgent reintubation may be required.

After conventional weaning and extubation to prevent postextubation failure

NIV application to all immediately postextubated patients had no impact on duration of ICU stay or reintubation rates.[118] However, Ferrer *et al.*[119] demonstrated in a RCT that when NIV was applied immediately after extubation to those patients, who had high risk of respiratory failure (age >65 yrs, APACHE II >12 at the time of extubation, cardiac failure at the time of intubation), it resulted in decreased reintubation and

ICU mortality in this group as compared to the controls. In a recent trial by the same author, they found that early NIV post- extubation diminished risk of respiratory failure and lowered 90-day mortality in patients with chronic respiratory disorders who developed hypercapnia during a spontaneous breathing trial.[120]

In another study, in high risk patients (patients who had hypercapnia, congestive heart failure, ineffective cough and excessive tracheobronchial secretions, more than one failure of a weaning trial, more than one comorbid condition, and upper airway obstruction) early application of NIV, immediately after extubation, is effective in reintubation and ICU mortality.[121] In a prospective observational study in pediatric patients, Mayordomo-Colunga *et al*.[122] concluded that postextubation NIV seems to be useful in avoiding reintubation in high risk children when applied immediately after extubation. NIV was more likely to fail when applied after development of respiratory failure and in neurologic patients.

When signs of respiratory failure develop after extubation

Hilbert applied NIV intermittently in 30 patients of COPD in whom postextubation failure occurred within 72 hrs. He found significant reduction in reintubation rates, duration of MV, ICU stay and mortality in patients, who also received NIV support as compared to those who received only medical therapy.[123]

Keenan *et al.*,[124] in a single center, prospective randomized study applied NIV to half the patients of a heterogeneous group who had postextubation failure within 48 hours. Although the duration of mechanical ventilation decreased in the NIV group, there was no significant reduction in mortality, reintubation rates or duration of ICU stay.

However a prospective, randomized, multicentre studies involving 37 centers from 8 countries, showed different results. 221 patients who developed post extubation failure within 48 hours were randomized for NIV vs. standard treatment. There was no difference in reintubation rates, which was 25% in each. Significantly, there was a trend towards a higher mortality in the NIV group (26 vs. 14%, $P = 0.48$). The median time from extubation to reintubation was also significantly more in the NIV group (12 hours vs. 2.5 hours $P = 0.02$). The higher mortality in the NIV group was attributable to the delay in reintubation, as 38% of those who were reintubated died in this group as compared to 22% in the standard treatment group ($P = 0.06$). There was a trend towards benefit of NIV in the subset of COPD patients but the patient number was too small for analysis.[125]

Recommendations

- NIV may be used to expedite weaning from invasive ventilation in uncomplicated cases of COPD who fail a trial of spontaneous breathing, but only in centres that have expertise in this therapy and an expertise always available for reintubation. (Level II)
- NIV can be recommended in patients after extubation who have a high risk of developing respiratory failure and reintubation and only in centres with expertise in this therapy. (Level I)
- We suggest that NIV should not be used after planned extubation in patients who are considered to be at low risk of respiratory failure (Level II)
- The use of NIV to reduce chances of reintubation in the event of post extubation respiratory failure in non-COPD cases is not recommended. It may, however, be used in COPD patients, but the evidence is still insufficient. (Level III)

Practice points

If NIV is applied for weaning from invasive mechanical ventilation or for postextubation failure in COPD, the following procedure could be adopted:

- A spontaneous breathing trial (SBT) should be given after at least 48 hours of stabilization on mechanical ventilation. If SBT is successful, extubate the patient
- If the patient fails SBT, then stabilize patient with full support on mechanical ventilation for I hour
- After stabilization, extubate the patient to NIV support
- Initially apply NIV continuously (22-24 hrs) with discontinuation only for feeding, drinking or expectoration
- Gradually, reduce time on NIV according to patient's requirement or by a validated protocol
- In cases of COPD who develop post extubation respiratory failure, NIV support should be applied only if there are no contraindications and the patient is compliant
- The above protocol is recommended only in ICU settings and in centers that have expertise in this protocol based therapy and a continuous specialist is always available for reintubation if required.

Contraindications

There are no absolute contraindications for the use of NIV. Some contraindications have, however, been suggested. Most contraindications have been determined by the fact that they were the exclusion criteria in many studies.[126,127]

- Inability to protect the airways - comatose patients, patients with CVA or bulbar involvement, confused and agitated patients
- Hemodynamic instability - uncontrolled arrhythmia, patient on very high doses of inotropes
- Inability to fix the interface - facial abnormalities, facial burns, facial trauma, facial anomaly
- Severe GI symptoms - vomiting, obstructed bowel, recent GI surgery
- Life threatening hypoxemia
- Copious secretions
- Conditions where NIV has not been found to be effective
- Non-availability of trained medical personnel
- Predictors of Success with Noninvasive Ventilation.

It is evident that not all patients with respiratory failure may be suitable for the successful application of NIV.[14,128,12] NIV has not been universally successful, with reported failure rates of 7-50% mainly due to the heterogeneity of the study populations.[29] It would appear, that those with a very mild form or very severe form of the disease do not benefit from NIV.[28] Justifiably, there are concerns about incorrect selection of patients leading to delay in instituting invasive ventilatory support. NIV is not a substitute for endotracheal mechanical ventilation, but only a way to prevent it by providing support early enough, before severe derangements take place.[30] Understanding the determinants of success will help in accurate patient selection for NIV and a timely switchover to invasive mechanical ventilation.

The following factors have been considered to influence immediate failure with NIV application:

- The baseline respiratory abnormalities at admission like respiratory rate, heart rate, pH and $PaCO_2$
- The severity of illness as assessed by APACHE or SAPS score
- Degree of encephalopathy as assessed by GCS score or the encephalopathy score
- Pre admission functional status as reflected by forced vital capacity (FVC) and the degree of restriction of the activities of daily living
- Inability to clear secretions
- Associated diseases such as pneumonia
- Response to NIV after its initiation
- Technical factors related to interface, mode and device used for ventilation, patient-ventilator synchrony, humidification and rebreathing and flow resistance.[130]
- Education and training of physicians and nurses involved in the use of NIV support.

Soo Hoo *et al.*[131] retrospectively studied a small number of patients? Who received nasal NIV? No differences in age, baseline pulmonary function or respiratory rate were found between those who succeeded and those who failed NIV. They also found that patients with hypercapnia at baseline did better as compared to those with hypoxemia alone.

In 17 consecutive patients with respiratory failure due to a variety of causes, Wysocki *et al.* found that those who were successfully ventilated with NIV had a higher pCO_2 and lower pH (7.33 vs 7.45) and a lower A-a O_2 difference at baseline.[132] However, Ambrosino *et al.*, on the other hand, in a retrospective review of a larger study of 59 episodes in 47 patients of COPD found that lower baseline PCO_2 values (79 vs. 98) and higher pH values (7.28 vs 7.22) correlated with success of NIV support. Keenan *et al.* in a recent systematic review of 15 randomized controlled trials observed that the benefit of NIV in COPD is demonstrable only in those with severe exacerbations and not in those with milder ones.[29]

The level of consciousness at admission has been used to predict success or failure. Most studies have excluded patients with altered sensorium due to theoretical concerns about the risk of aspiration. Guidelines have also cautioned against its use in the presence of altered consciousness.[5] Anton *et al.*[134] studied 44 episodes of exacerbations in 36 patients of COPD and confirmed the findings of Ambrosino *et al.*[133] that baseline level of consciousness and pH values correlate with success. Several studies have however demonstrated success with NIV in the presence of altered sensorium and even coma.[135,136] Benhomou achieved a success rate of 65% even in those with severe respiratory acidosis and encephalopathy.[137] Diaz *et al.* showed that patients in hypercapnic coma with GCS <8 can be treated as successfully with NIV.[23].Similar observations were reported by Mani who found that intubation could be avoided even with encephalopathy at baseline and initial rise of PCO_2 on NIV[138].This was achievable if there was no deterioration of consciousness. in the initial hours of application of NIV support.

Plant *et al.* in a large, multicentric, prospective study concluded that lower PCO_2 and higher pH levels after 2 hrs NIV support correlated with success and that it is possible to calculate the risk for intubation based on these and other values.[128]

In a prospective, randomized controlled trial Confalonieri found that in the subgroup with COPD, the 2 month survival rate was better in these who received NIV than in those who received conventional treatment alone.[60] Baseline APACHE scores were found to have no significant impact on the outcome with NIV, although its efficacy differs in various disease conditions. Plant *et al.*, however, in a prospective multicentre study found correlation of APACHE >29 with failure of NIV.[128]

Response to NIV may also indicate the chances of success. Studies appear to indicate that this can be gauged early within the first 2 hours. Ambrosino *et al.* went on to suggest that those who did not improve within 1-2 hrs in terms of PCO_2 and pH values should be intubated.(133) Carratu *et al.*[140] have shown that patients who improve have increased pH and decreased $PaCO_2$ at 2 hours post NIV whereas those who fail have no change in these two parameters. Other predictors of early failure were a low pH, low GCS and higher APACHE II scores. In a failure risk model for NIV in COPD, Confalonieri *et al.*[140] have recently shown that a GCS <11, APACHE >29, respiratory rate more than 30 and pH <7.25 predicted a 50% failure risk and a pH of less than 7.25 at two hours post NIV predicted a 90% failure risk.

Several other studies have adopted short-term (1-4 hours) trials to predict failure and indeed most guidelines advice this.[5,57,135,139,141,142] Benhomou noted that the only factor that determined outcome was the tolerance to the mask.[137] Similarly, Ambrosino found compliance to be an important factor. Air leak is another factor recognized to be important.[133]

A late failure, i.e., respiratory failure occurring after 48 hrs of support with NIV has been recognized. Moretti *et al.*[143] found that 23% of patients deteriorated late. When those who refused intubation were then given more aggressive NIV, they did worse in the in-hospital period than those who had accepted invasive ventilation (mortality of 93% compared to 52%). Patients with late failures had significantly lower activities of daily living (ADL) scores, lower pH and associated complications at admission.

In a prospective study of 27 hypercapnic patients, Campo *et al.* concluded that late NIV failure in elderly patients was associated wth early sleep disturbances including abnormal EEG pattern, disruption of the circadian sleep cycle and decreased REM sleep.[144]

Recommendations

- NIV is likely to succeed in patients with exacerbations of COPD of more than mild severity and in selected cases of hypoxemic failure. (Level I)
- NIV may be applied when established contraindications are absent, in all patients where it is indicated, irrespective of age, baseline APACHE score, degree of chronic respiratory disability and pre-intervention pH or $PaCO_2$. (Level II)
- After NIV initiation, deterioration of clinical and arterial blood gases in the initial (1-4) hours predicts failure and calls for an early switch to invasive ventilation. (Level II)
- Presence of encephalopathy in COPD may not predict failure of NIV. However, failure to improve with NIV in few hours suggests failure. (Level II)
- Presence of pneumonia in patients of COPD does not preclude a trial of NIV. (Level II)
- Patient's intolerance of mask, poor compliance or the presence of excessive air leak predicts failure of NIV. (Level III)
- (Level II. In the event of late failure I).

Practice points

- NIV should be discontinued if the patient is unable to tolerate the mask despite best efforts or does not accept this form of support. Such patients should receive invasive support early
- In edentulous patients who are awake and able to protect their airway, dentures should be placed in the mouth to ensure a good mask fit and to minimize air leak
- Monitor RR, HR and BP, level of consciousness, pH, pCO_2 and pO_2/SpO_2 closely in the initial hours after NIV initiation in order to detect early signs of failure
- In case of deterioration of the above parameters in the initial few hours, discontinue NIV and initiate invasive ventilation without undue delay
- Risk of failure is high in hypoxemic respiratory failure
- ARDS is an independent risk of failure.

Application of noninvasive ventilation

Modes of noninvasive ventilation

All modes of ventilation that are used invasively can theoretically also be used for applying noninvasive ventilation. However, NIV is usually delivered in the form of assisted ventilation where every breath is supported. Rarely however, controlled mechanical ventilation used.[145]

There are four principal modes in which noninvasive ventilation can be used:

Controlled mechanical ventilation

Patient's breathing effort is not required and the ventilator provides full ventilatory support. On the NIV machines, this mode is referred to as 'timed' mode (T).

Assist control ventilation

Assist control ventilation not only assures full ventilatory support to the patient but also allows spontaneous breathing efforts by the patient. This mode provides back-up safety rate, should the patient not trigger the ventilator. This mode is referred to 'spontaneous/timed' mode on NIV machines (S/T).

Assist mode

Ventilator augments the inspiratory effort made by the patient. Assist mode doesn't provide back-up safety rate, should the patient not trigger the ventilator. Therefore assist mode will work only if the patient is able to trigger the ventilator with his own effort. This mode is referred to 'Spontaneous' mode on NIV machines (S).

Continuous positive airway pressure

A constant pressure is applied to the airway throughout the respiratory cycle. This mode doesn't provide inspiratory support, so the patient should have the capacity to breathe spontaneously. This isn't a mode of mechanical ventilation in true sense and used mainly in hypoxemic respiratory failure due to cardiogenic pulmonary edema.

Proportional assist ventilation

The ventilator assists the patient by generating volume and pressure in proportion to patient's effort, creating a ventilatory pattern that matches metabolic demands on a breath-by-breath basis. Till date, there is no data to show any advantage of PAV.

Equipment to be used for NIV and its Maintenance

Ventilators

Conventional ICU ventilators with full monitoring and alarm systems, portable volume preset ventilators and portable pressure preset ventilators have all been used for providing NIV.

The advantages of typical ICU ventilators are the presence of full alarm systems, ability to deliver a precise/high FiO_2 and the ability to prevent rebreathing. Newer NIV ventilators incorporate many of these features for their use in the acute care setting, albeit at significantly increased cost. Portable non-invasive ventilators and conventional critical care/ICU ventilators are equally effective when used for NIV. in particular ventilators with oxygen blenders are preferred for patients with hypoxemic respiratory failure.[145-147]

NIV ventilators can be basically classified into pressure or volume preset, though some models incorporate both the modalities in a single machine. In volume-preset ventilation, the set parameter is the tidal volume delivered and airway pressure is variable depending on lung characteristics. In pressure-preset ventilation, the set parameter is the applied airway pressure and tidal volume delivered is variable.

Pressure preset ventilation could be either pressure controlled or pressure support. In pressure controlled ventilation the delivered pressure and the time for which it is applied is preset. In pressure support ventilation, the applied pressure is preset but the duration for which it is applied is dependent on the patient effort. Pressure support breath is terminated when the flow rate decreases to a predetermined percentage of the initial flow rate. Although the concept of NIV was started with the use of volume-preset ventilators, pressure preset ventilation is now the predominant mode used in NIV.

NIV ventilators providing bilevel positive airway pressure ventilation are the most popular. These machines deliver two treatment pressures. A higher pressure is applied when the patient inhales and is called IPAP (inspiratory positive airway pressure) and a lower pressure is applied when the patient exhales called the EPAP (expiratory positive airway pressure). The difference between these two pressures is the effective pressure support. EPAP is equivalent to applying PEEP in a spontaneously breathing subject.

The advantage of volume-preset ventilators is that they provide a relatively constant tidal volume in the face of changing lung characteristics (increasing airways resistance/worsening lung compliance) whereas with pressure-preset machines the tidal volume will vary with changing lung characteristics.

The advantage of pressure-preset machines is that they compensate for leaks, which are common in patients on NIV, either from the mask or the mouth. Most pressure-preset machines also offer facility for EPAP, which has advantages in certain patients. The peak airway pressure can also be limited unlike volume-preset machines, which do not limit peak pressure. This can create problems of gastric distension and barotrauma in certain susceptible patients (bullous lung disease). Another great disadvantage of volume-preset machines is that the flow is fixed and if the flow demand of the subject is greater, then it will lead to 'flow starvation' and consequently patient ventilator asynchrony. In pressure-preset machines, flow will vary according to patient's demands making it easier for a subject to synchronize with the ventilator. Volume preset machines also tend to be more bulky and costlier when compared to their pressure counterparts, which are lighter and more portable.

There have been a number of studies comparing volume and pressure preset machines in various groups of patients. Pressure preset ventilation has been shown to be as effective as volume preset ventilation in terms of improving breathing pattern and gas exchange parameters.[148-152] Pressure preset machines are also simpler to use, lighter and cheaper. Lab studies using lung models have also shown the better leak compensation ability of pressure-preset ventilation.[153]

The choice of a machine providing assist or assist control mode depends on the patient's disease severity.[154,155] In sick patients, who are being ventilated for acute respiratory failure, a machine with assist/control facility is desirable whereas a machine with only assist mode could ventilate a stable patient with chronic respiratory failure on domiciliary ventilation. There is a substantial cost difference between these two types of machines. Staff familiarity and training with the ventilator is an important determinant of success and it is desirable to use a single model of ventilator in a particular area.

Use of EPAP/bi level machines

- The ability to provide an EPAP on pressure-preset ventilators is advantageous. Unlike ICU ventilators, which separate inspiratory and expiratory gas mixtures, portable ventilators used for NIV have single tubing with a potential for rebreathing expired gas[156]
- The application of EPAP flushes dead space CO_2 and prevents rebreathing
- EPAP also helps in alveolar recruitment, prevents atelectasis and stabilizes the upper airway during sleep
- EPAP has been found to be more useful in improving gas exchange parameters in patients with chest wall/ neuromuscular disease as compared to patients COPD[157]
- In patients with COPD who have significant intrinsic PEEP, EPAP can offset this iPEEP, decrease the work of breathing and improve trigger sensitivity.[158]

Triggering

- Triggering or changeover from expiration to inspiration is crucial for the success of NIV. A ventilator that triggers to the inspiratory phase in a very sensitive manner, thereby responding to patient's efforts, prevents ventilator-patient dysynchrony. At the same time, it should not be so sensitive that it auto-triggers[159]
- An effective trigger is crucial for the success of NIV, particularly in acute respiratory failure.[160] Both pressure and flow triggering have been used and no clear superiority of one mode over the other has been established. In patients with COPD, flow triggering, by ensuring a constant flow through the circuit, does reduce the amount of auto-PEEP thereby ensuring some advantage for flow triggering.[161] In general, flow triggered devices appear to be more sensitive than pressure triggered devices and are associated with a lesser work of breathing.[162]

Pressurization

- The ventilator should have the ability to meet the flow demand of the patient. Flow demand depends mainly on the resistance and compliance or the underlying pathology. Gas flow can be increased either by increasing inspiratory pressure support or by reducing pressure rise time.[160]

Cycling

- Cycling or changeover from inspiration to expiration, in harmony with the patient's breath, is another important function that a good ventilator must be able to perform
- Cycling is also called expiratory triggering. The criteria used for expiratory triggering can have an impact on the efficiency of NIV and patient-ventilator synchrony. The usual criterion used in pressure support ventilators is a decrease in inspiratory flow from a peak to a threshold value (for example 25% of peak flow). This varies amongst various NIV machines. Since most patients with COPD or air leaks have high end inspiratory flows, a high flow threshold (25 to 40%) should be chosen for these patients as a lower threshold may lead to prolonged inspiratory times
- Ventilators with a facility for adjustable maximal inspiratory times also permit better patient-ventilator synchrony. Settings the maximal inspiratory time (Ti) at one second is a reasonable approach. When patients with COPD have air leaks, the ventilator does not decrease the inspiratory flow, thereby not allowing the decrease in inspiratory flow, which cycles the machine to expiration. This leads to prolonged inspiration and patient-ventilator dysynchrony. By setting the inspiratory duration to no more than half the respiratory cycle duration, this effect can be minimized.[158,163] Therefore, machines with adjustable expiratory triggers offer advantages.

Alarms

- Alarms on non-invasive ventilators are basic and detect disconnection (low pressure alarm), high pressure, worsening leaks (flow alarm) and power failure. More sophisticated alarms add to the complexity and cost of machines. As NIV is used on more stable patients than conventional ventilation, a whole lot of alarms are not needed.

Oxygen administration

- Supplemental oxygen can be administered by connecting oxygen directly to a port on the mask or to a T-connector in the ventilator circuit. Unlike classical ICU ventilators, non-invasive ventilators lack the ability to deliver precisely controlled oxygen-air mixtures to patients. The FiO_2 will vary according to the patient's respiratory pattern. High levels of FiO_2 cannot be achieved because of dilution by base flow (EPAP). One can only achieve a high Fio_2 with ICU ventilators. The best way to monitor oxygen administration is by pulse oxymetry.

Humidification

- As physiological humidification mechanisms are unaltered in NIV and much of the air being breathed is ambient and consequently better humidified, humidification is not routinely needed. It may be useful in patients with thick or tenacious secretions and patients who develop nasal stuffiness, dryness and congestion. It can be provided with simple or heated pass-over humidifiers, a pass-through humidifier or a heat and moisture exchanger. Whereas the first two require an extrinsic water source, heat and moisture exchangers reuse the moisture in the expired air for humidification. It is important to remember that these devices can alter the triggering characteristics of the ventilator and caution needs to be exercised. This problem occurs least with pass over humidifiers
- It is important to remember that air leaks will produce increase in the base flow with consequent more nasal symptoms and rectification of the air leak by appropriate methods alone can circumvent the need for additional humidification.[165]

Sedation during NIV

- Patient agitation is a relative contraindication for NIV. Sedation helps in reducing anxiety and respiratory rate but it must be administered with caution in a monitored setting. Benzodiazepines and opioids are the most commonly used agents but dexmedetomidine is useful in agitated patients as it decreases agitation without inducing respiratory depression.[166]

A basic ventilator-designed specifically for NIV should therefore comprise the following features:

Pressure preset-pressure support

- Capable of providing pressures at least upto 25 cm H_2O
- Capable of generating high flows for meeting patient inspiratory flow demand (60-100 LPM)
- Should ideally have spontaneous timed option
- Sensitive trigger, preferably flow based
- Lightweight/portable
- Basic alarms
- Capable of supporting a breath rate of at least 40 breathes per minute
- Additional desirable attributes include adjustable pressure rise time (ramp), adjustable inspiratory and expiratory triggers, battery backup, simple control knobs and ability to prevent inadvertent change of parameters (cover or lock out facility).

Recommendations

- Both ICU ventilators and portable NIV ventilators can provide NIV. Portable pressure preset bilevel ventilators are advantageous in terms of patient comfort. They are also less expensive, lightweight and easier to maintain. (Level III)
- Staff familiarity with the ventilator is important in outcome and it is desirable that one area be equipped with one particular model for ease of training. (Level III).

Patient ventilator interface

Interfaces are devices that connect the ventilator tubing to the patient and facilitate the entry of pressurized gas into the upper airways during NIV. Choice of interface is a major determinant for NIV success or failure. The various interfaces available include-Nasal mask, Oronasal mask, Full face mask, Mouth piece, Nasal pillows and Helmet.

Oronasal mask is the most commonly used interface for respiratory failure, followed by nasal mask, helmet or mouth piece. They are available in multiple sizes to suit pediatric and adult patients. It is very important to choose appropriate sized interface, (small, medium, large, wide or narrow) as it strongly affects patient’s comfort and influence the development of NIV problems.[168]

The advantages of nasal mask include less dead space, less claustrophobia and minimum complications especially if vomiting occurs. However, full-face masks are used in acute respiratory failure since very dyspneic patients are mouth breathers. It is especially important to remember that full-face masks can add substantial dead space with consequent risk of rebreathing expired gas mixtures.[168] they also tend to be more claustrophobic. There are not enough published studies to make firm recommendations and there are not many patients' tolerance direct comparison studies of efficacy. Anton *et al.* compared the efficacy and patient tolerance of nasal and full facemasks during acute exacerbations of COPD. They concluded that NIV improves ABG and respiratory indices regardless of type of mask used.[169] Navalesi *et al*. compared the efficacy of NIV using nasal and full facemasks in patients with chronic respiratory failure. They found that the nasal mask was better tolerated, though the minute ventilation was significantly higher and $PaCO_2$ was significantly lower with a full facemask.[169] Studies in patients with acute hypercapnic respiratory failure have shown an overall bias in favor of a facemask in producing quicker improvement in blood gases. A recent randomized controlled trial comparing nasal and oronasal masks found both to be equally efficacious in the reduction of $PaCO_2$ or respiratory rate in patients with acute respiratory distress, though the full facemask was better tolerated.[171]

Recently, a novel interface, a helmet, has been described, which is a clear plastic cylinder that fits over the head and seals with straps under the shoulders. It does not seal the nose and mouth, thereby improves comfort. Two studies have compared CPAP via helmet in patients of hypoxemic respiratory failure with historically matched controls who used standard full-face masks. Both studies found that the helmet permitted more prolonged delivery of CPAP and was better tolerated.[172,173] However, in patients with hypercapnic respiratory failure due to COPD, the helmet appeared to be less efficient.[174]

In a recent study by Fodil *et al.*, it was found that between different interfaces the effective dead spaces differed only modestly (110 to 370 ml) while their internal volumes were markedly different (110 to 10000 ml).[175]

A variety of mask accessories are available that optimize mask fit, comfort and prevent troublesome side effects like nasal bridge pressure sores and leaks. Mask templates are available for sizing masks for individual patients. Choice of headgear or the strap that hold the mask is especially important and an element of elasticity must be present in the headgear material to prevent undue tension on the subject's skin, especially the nose. Mask cushions help in increasing comfort and preventing leaks and excessive pressure on the skin. Foam spacers aid in prevention of nasal bridge pressure sores by transferring pressure onto them. Elastic chinstraps are particularly useful in preventing air leaks through the mouth. Masks with anti-asphyxia valves permit breathing, if the ventilator stops functioning. The range of accessories is large and their optimal use is best learnt by continuous practice of NIV.

Mask selection

Exhalation devices

- A variety of exhalation devices are available which vent the expired air to the exterior and also introduce an intentional leak in the system to flush the mask and circuit, thereby preventing rebreathing. These could either be simple exhalation ports built into the mask or could take the form of a separate attachment in the circuit (simple swivel valves, disposable exhalation ports or non-rebreathing valves)
- It is important to remember that CO_2 rebreathing can occur with NIV using standard exhalation valves. Moreover, masks add significant dead space. If a patient while on NIV has unexplained rise of CO_2 or non-improvement of CO_2, this possibility should be considered
- This problem can be tackled by either using a non-rebreathing valve or by increasing the level of EPAP, which flushes the mask and circuit. However, it is important to remember that at commonly used levels of EPAP, especially when the respiratory rate is high, a substantial rebreathing volume may still be present.[176] Because the ventilators trigger algorithm takes leak flow into account, only breathing circuits, exhalation valves and masks that are recommended by manufacturer should be used.

Recommendations

- Both nasal and full-face masks can be used for providing NIV successfully. However, in the acute setting full-face masks appear to be advantageous. (Level I)
- A unit should be equipped with a range of masks and accessories since the interface is crucial to the success of NIV. (Level III)
- A proper exhalation device should be used because of a possibility of rebreathing during NIV and worsening hypercapnia. (Level III).

Maintenance

All ventilators should be maintained strictly according to the manufacturer's recommendations. This includes both preventive maintenance and rectification of faults by qualified personnel. Care of the ventilators should be delegated to a specified person and all ventilators when not being used should be parked in a single designated area of the hospital. An inventory of equipment should be maintained.

Since most ventilators have a base flow (EPAP) even during expiration, there is no airflow from the patient back into the ventilator. Therefore the risk of contamination of the ventilator is extremely low, especially when an outlet bacterial filter is being used.

Superficial cleaning of the ventilators exterior with a slightly dampened cloth and a mild detergent between patient uses is satisfactory. Unplug the unit before cleaning. Ensure that the unit is dry before plugging it in. Do not use bleach, chlorine or alcohol based solutions to clean the exterior of the ventilator.

The air inlet filter on the ventilator should be regularly inspected to see if it is blocked by dirt or contains holes and replaced when it appears dirty. There is no firm limit of time in which the filter has to be changed since the life of the filter will depend on the dust in the ambient atmosphere. Follow the manufacturer's recommendations regarding the time frame for change. The filter must be changed when the unit is unplugged. Under no condition, should the unit be running without a filter in place. Only the filter recommended by the manufacturer should be used. Failure to replace a dirty filter may cause drop in ventilator flow and pressures and may elevate the operating temperature of the machine with consequent damage to the sensitive ventilator internal circuitry. All filters are disposable and must not be reused after washing.

A ventilator performance verification check should be performed periodically and preferably before use in each new patient to see if the ventilator is adequately pressurizing. The aim is to see whether the ventilator is indeed pressurizing the circuit at the same level as set on its control. This can be done in ventilators with a built in pressure monitor or a simple hand held commercially available manometer. This can be done by occluding the circuit outlet and measuring the pressures at the outlet and ensuring that the pressure matches with that set on the machine. This should be done at different settings of pressure, for example, at 5 cm, 10 cm, 15 cm of IPAP and EPAP. This should be done in all the modes available on the ventilator. The triggering and cycling function of the machine should be checked in all the modes (S, S/T and T). By creating a small leak in a circuit to simulate a trigger, the cycling from IPAP to EPAP can be verified. It is also important to see whether the unit cycles at the set rate on the BPM control in the S/T and Timed modes.

If the ventilator is equipped with alarms, verify the functioning and responsiveness of the alarms and their settings. If an outlet filter is being used, it is important to know its resistance characteristics. The pressure at the mask port should be verified when the ventilator is in use to see if the filter is causing any pressure drop in the circuit.

Ventilator accessories like fuses and batteries should be replaced strictly following the specifications and procedures as described by the manufacturer. No unqualified personnel should be allowed to service or repair the unit. Electrical safety checks should be undertaken at least once a year. It is helpful to have a maintenance schedule so that planned preventive checks can be undertaken. An annual maintenance contract with the manufacture is recommended.

Accessories

All accessories stamped, as single use should not be recycled amongst patients. Masks and exhalation valves require high-level disinfection between patients. The manufacturer's recommendations should be strictly followed as regards to the nature of the disinfecting agent. Both heat (dry-pasteurization, moist-autoclaving) and chemical methods (per acetic acid, glutraldehyde) are used. While using heat, it is important to know the temperature, duration of exposure and type of heat used. While using chemical disinfection, it is important to know the type of chemical and its concentration and exposure time.

Cleaning and disinfecting of accessories

It is not recommended to re-use disposable interfaces. The following recommendation is only for re-usable interfaces. Re-usable masks should first be cleaned, prior to using any disinfection or sterilization method.

Steps

- Remove the headgear and spacer
- Soak the parts in a commercially available enzymatic cleaner
- Clean the mask with a soft bristle brush in a solution of cool tap water and a commercially available ammonic detergent. Do not use cleaning products that contain conditioners or moisturizers because they will leave a residue
- Rinse thoroughly under cool running tap water and then air dry
- Disinfection/Sterilization process can be done by following the manufacturers recommendation
- If adhering substances cannot be adequately removed, replace the mask
- Reusable ventilator tubing is difficult to sterilize by

these methods because of its long length and should preferably be autoclaved

- All fabric accessories (headgear, chin straps) should be washed at 65 degree centigrade cycle for 10 minutes and dried before use. This cycle is available on most washing machines. Drying of all masks and accessories should take place in room air and not in sunlight. Automated combined washing/ disinfecting/ drier systems are available, though they add cost.

Recommendations

- Each unit should have a person designated for maintenance of ventilators. Qualified personnel should do preventive maintenance according to the manufacturer's recommendations (level III)
- Parts labeled, as single use should not be recycled. Reusable parts should be disassembled into components, washed to remove organic matter and subjected to high-level disinfection strictly following the manufacturer's recommendation (level III).

Practice points for equipment

- Clinicians must be fully aware of the various characteristics (trigger, cycling, ramp etc) of their NIV machine and should use them optimally for better patient-ventilator synchrony
- It is desirable to lock the set parameters to prevent inadvertent change by staff or attendants
- For patients not showing the expected fall in CO_2 levels, the problem of rebreathing of expired breath should be considered
- A full range of accessories should be available for optimal ventilator-interface synchrony. These add some cost but are helpful in improving efficiency of ventilation. In particular, elasticized headgear should be used to prevent pressure sores on the nose/face
- It is highly desirable to use the circuit tubing, masks and exhalation devices recommended by the ventilator manufacturer as this can affect ventilator performance
- A protocol for ventilator maintenance and sterilization should be in place. The ventilator operator manual and the manufacturer's website provide rich information.

Practical application

Patient selection

The success of NIV depends on selecting the right patient. This process should take into account the diagnosis, clinical status of the patient, risk of failure and clinical judgment of the caregiver. One must also consider the evidence supporting the effectiveness of NIV in that particular patient.

It has been recommended that the need for ventilation according to clinical criteria must first be established [Table-1].

Table 1: Clinical criteria

Moderate to severe respiratory distress
Tachypnea, (respiratory rate >25/min)
Accessory muscle use or abdominal paradox
Blood gas derangement pH <7.35, $PaCO_2$ >45 mmHg
PaO_2/FiO_2 <300 or SpO_2 <92% with FiO_2 0.5

Practice points

Application of NIV using portable pressure ventilator[177]

- Choose the correct interface
- Explain therapy and its benefit to the patient in detail. Also discuss the possibility of intubation
- Set the NIV portable pressure ventilator in spontaneous or spontaneous/timed mode
- Start with very low settings. Start with low inspiratory positive airway pressure (IPAP) of 6-8 cm H_2O with 2 to 4 cm H_2O of EPAP (Expiratory positive airway pressure). The difference between IPAP and EPAP should be at least 4 cm H_20
- Administer oxygen at 2 liters per minute
- Hold the mask with the hand over his face. Do not fix it
- Increase EPAP by 1-2 cm increments till all his inspiratory efforts are able to triggers the ventilator
- If the patient is making inspiratory effort and the ventilator does not respond to that inspiratory effort, it indicates that the patient has not generated enough respiratory effort to counter auto PEEP and trigger the ventilator (in COPD patients). Increase EPAP further till this happens. Most of the patients require EPAP of about 4 to 6 cm H_2O. Patient who are obese or have obstructive sleep apnea require higher EPAP.
- When all the patient's efforts are triggering the ventilator, leave EPAP at that level
- Now start increasing IPAP in increments of 1-2 cm up to a maximum pressure, which the patient can tolerate without discomfort and there is no major mouth or air leak
- In some NIV machine, inspiratory time (Ti) can be adjusted. Setting the Ti at one second is a reasonable approach
- Now secure interface with head straps. Avoid excessive tightness. If the patient has a nasogastric tube put a seal connector in the dome of the mask to minimize air leakage
- After titrating the pressure, increase oxygen to bring oxygen saturation to around 90%
- As the settings may be different in wakefulness and sleep, readjust them accordingly.

When NIV is being initiated for acute respiratory failure, close monitoring and the capability to initiate endotracheal intubation and other resuscitation measures should be available in the same setup. Start NIV preferably in the ICU or in the emergency room in acute respiratory failure.

Application of NIV using a critical care ventilator

- The first step is to select a ventilator, which is capable of fulfilling the needs of the patient
- Explain the therapy to the patient
- Choose the appropriate mode. Usually pressure support or pressure control modes are preferred. Standard critical care ventilators using flow by system allow the patient to breathe without expending effort to open valves. In selected patients like those suffering from neuromuscular diseases, volume assist or volume control mode may be used
- Choose an appropriate interface
- Keep FiO_2 0.5.

Using pressure approach

- Start with low settings like inspiratory pressure support at 5-6 cm H_2O and PEEP at 2 cm H_2O
- Initiate NIV while holding the mask in place and confirm optimum fit. If it is big or small or loose, change it
- Secure interface with headgear or hold mask. It should be tight, but not over-tight. Small leaks are acceptable
- Now increase PEEP till all his inspiratory efforts are able to triggers the ventilator
- If the patient is making inspiratory effort and the ventilator does not respond to that inspiratory effort, it indicates that the patient has not generated enough respiratory effort to counter auto PEEP and trigger the ventilator (in COPD patients). Increase PEEP further till this happens
- Once the patient's all inspiratory efforts are triggering the ventilator then start increasing pressure support further, keeping certain patient' comfort in mind. (Reduce respiratory rate, reduced use of accessory muscle etc., Ensure that there are no major leaks
- When there is significant mouth leak, there may be asynchrony. In that case, pressure control will be the preferred mode of NIV and one can set up the inspiratory time to avoid asynchrony
- After adequate ventilation has been achieved, increase fraction of oxygen concentration to maintain Oxygen saturation more than 90%
- A peak inspiratory pressure more than 25 cm is rarely required in COPD, but higher pressures can be used when using NIV for other indications. PEEP is usually titrated between 5-10 cm H_2O to improve triggering and oxygenation.

Monitoring

Monitoring is important not only for optimizing ventilator setting, but also to warn against impending catastrophe if NIV fails.[127]

Subjective response

- Once NIV is successfully initiated the smooth adaptation of the patient to the ventilator is very important
- One should try to make the patient comfortable by loosening the head strap or changing the interface. NIV should alleviate his symptoms like dyspnea. Once the patient is more comfortable, he tolerates NIV better.

Physiological response

- Simple vital sign should show an improvement. These can be assessed by examination of chest wall movement, heart rate, respiratory rate, mental state and patient coordination with the ventilator. One of the first signs of a good response to non-invasive ventilation is a drop in the respiratory rate within a first few hours. Evaluation of the patient ventilator synchrony is difficult without visualization of flow and pressure waveforms
- This is possible in ICU ventilators with graphic displays and advanced NIV ventilators. Air leak and patient ventilator asynchrony should be monitored and corrected as and when required and one must remember that the tidal volume displayed may be misleading, particularly during use of bi-level ventilators. The readout is usually inaccurate in the presence of air leaks.

Adequate gas exchange

- Oxygen Saturation or pulse oxymetry in the acute setting is a most fundamental measurement and should be maintained >90%. ABG is used to judge the effectiveness of noninvasive ventilation. In acute respiratory failure, ABG should be checked at baseline and at 1-4 hours
- A number of studies have shown that improvement in arterial blood gas tensions particularly in pH, after a short period of NIV predicts a successful outcome.[5,57,136,142] It is recommended that ABG be done at least once a day in stable patients. Before discontinuing NIV, the patient's ABG without NIV for one hour may be a good guide to predict weaning from NIV.

Problems and complications

NIV is both safe and well tolerated in both acute and chronic settings, when applied in appropriately selected patients. However, there can be problems, which can be solved by judicious application of NIV.

Problems related to the interface

- Interface related problems are the most commonly encountered complications of NIV. An improperly fitting mask and excessive strap tension cause discomfort (30-50%), nasal bridge redness (5-10%), feeling of pressure over nose[5] and claustrophobia (5-10%). The discomfort at the point of skin contact is related to the strap tension necessary to control air-leak. Pressure sores occur when excessive pressure is applied for too long[178-180]
- Patient should be clinically evaluated at each mask change for trigger-sensitivity and pressure settings. (Reference required).

Practice points

- The smallest size mask that just encompasses the nose is usually the best nasal mask.
- Forehead spacers should be used and replaced regularly to redistribute pressure away from nasal bridge.
- Strap tension should be adjusted so that no fewer than two fingers can be accommodated under them.
- Use elasticized head straps.
- A barrier dressing over the nasal bridge may be used from the outset to reduce risk of complications.
- If ulceration occurs over nasal bridge, artificial skin ('Duoderm') may be applied to the area for greater protection.
- When NIV is being initiated just hold the mask (without the strap being tied) on the nose or face for a few minutes so that the patient gets adjusted to the pressure and does not feel claustrophobic. Though this is time consuming, it helps in increasing mask tolerance.
- Some leak is inevitable. If the patient is able to trigger the ventilator, accept a small leak.
- Full face mask may be advantageous in patients who are unable to tolerate a nasal mask due to some nasal pathology.

Problems associated with air pressure and flow

- Air Pressure and Flow can cause minor problems, which can be managed with simple measures.
- Leaks large enough to render NIV ineffective have been reported in only a minority of patients.[165,166] Air pressure in nose and sinuses may cause pain, burning, coldness or ear pain (10-30%), nasal congestion (20-50%) and dryness (10-20%). Oral dryness can be caused by a air leak through mouth. High nasal airflow related to air leaking through the mouth increases nasal resistance.[165]
- Gastric distension can occur in some patients but is rarely intolerable.
- Air leak on the side of nose may also cause eye irritation. Excessive tightening of mask strap could be responsible for this.

Practice points

- Use correct sized mask and headgear to minimize leak
- In acute respiratory failure, use full-face mask to prevent for excessive mouth leak
- Initiate NIV with relatively low inspiratory pressure (6-8 cm H_2O) and then titrate upward as tolerated.
- For nasal congestion, use topical nasal steroids or anti histamines
- For nasal dryness, use topical saline or emollient spray
- Oral dryness responds to reducing mouth leak. One may use a chinstrap or change to full-face mask
- Intermittent nebulization with saline can help in humidification]
- Humidifiers may increase ventilator circuit resistance, interfering with triggering and rendering ventilator pressure settings inaccurate; hence their use should be avoided.[5]
- Simethicon may help in gastric distension
- Adjust the strap, use soothing eye drops or use bubble mask for eye irritations.

Problems associated with intolerance to NIV

- Intolerance to NIV may be due to mask intolerance or patient ventilator asynchrony. Improper size or fitting of mask and excessive strap tension are the important reason for mask intolerance
- Patient - ventilator asynchrony in NIV was observed when PSV mode was used and there was a major air leak. 10-15% of patients are not able to tolerate the sensation of foreign body on the face or the airflow.

Practice point

- Intolerance should be dealt with patience and persistence
- Adjustment in EPAP may help in patients with presumed auto PEEP
- Adjust inspiratory support to assure adequate inspiratory time. Use of ventilators that allow setting of inspiratory trigger sensitivity and a shorter

inspiratory duration (0.5-1.5 sec) may ameliorate asynchrony
- Reassure and encourage the patient. Suggest to the patient to let the machine breathe for him.

Problems associated with failure to ventilate adequately

- Failure to ventilate could be due to air leaks, rebreathing, poor patient compliance or progression of the primary disease.
- Air leak: There is no airtight conduit with NIV hence it is not possible to achieve a leak free assembly.
- CO_2 rebreathing: The BiPAP and other bi-level ventilators use bias flow during exhalation to flush exhaled CO_2 out through an exhalation valve. Ferguson and Gilmartin[156] have demonstrated that rebreathing may interfere with the capability to lower CO_2 when used with certain expiratory valves at a low expiratory pressure. Swivel exhalation valve (BiPAP) has been shown to prevent rebreathing when expiratory pressures are <4 cm H_2O
- Position of exhalation port affects dynamic dead space. Port over nasal bridge is the best in this regard followed by that elsewhere within the mask and those in between mask and ventilator circuit.
- In patients with advanced restrictive thoracic and parenchyma lung diseases or progression of primary disease, the set support may be inadequate and may need to be increased.

Major complications

Major complications are infrequent (5%) if the patient is appropriately selected. They include:
- Delay in intubation and worsening of prognosis
- Major desaturation and cardiac arrest in hypoxemic respiratory failure
- Aspiration pneumonia occurs in up to 5% of patients. It is most often seen in patients who are reluctant or decline to undergo endotracheal intubation and may have some impairment of airway protective mechanisms but desire trial of NIV
- Hypotension: Is infrequent among appropriately selected patients. In case the patient has inadequate intravascular volume or underlying cardiac disease, the mild increase in intrathoracic pressure may decrease venous return and cause hypotension. Development of auto PEEP is another reason for causing hypotension in COPD patients[127]
- Pneumothorax may occur in patients with bullous lung disease. The bullae may rupture and produce pneumothorax if high insufflation pressures are used (>25 cm H_2O).[178] When CPAP/BiPAP is used in patients with rib fractures there is a risk of developing pneumothorax which is similar to that occurring in invasive ventilation.

Practice point

- Exclude patients with compromised upper airway function or those who have a problem clearing secretions
- Do not permit at risk patients anything by mouth till they are stabilized. Use of nasogastric or orogastric tubes in these patients is undesirable
- Adequate hydration of the patient must be assured. In patients with pulmonary edema begin with CPAP alone or bilevel ventilation using low inflation pressures (11-12 cm H_2O - IPAP; 4-5 cm H_2O EPAP) while monitoring clinical response.[62]
- Use of NIV should be avoided in patients with uncontrolled ischemia or arrhythmias until these problems are stabilized
- Inspiratory pressures should be kept at minimum effective level in patients with bullous lung disease. Patients with chest wall trauma who are being treated with NIV or CPAP should be monitored in ICU.

Location of NIV

It is understandable that various countries have different standards of care and definitions of ICU, high dependency unit (HDU) and general ward. Even in our country, model of hospital care varies from city to city. Different patterns of staffing, facilities, resources, degree of training and monitoring systems may be prevalent in ICUs, HDUs and general wards. For discussion purposes on NIV we will define these areas as mentioned below:
- Intensive care unit: ICU is a unit with high ratio of medical staff to patient. Facilities for invasive ventilation and invasive/noninvasive monitoring are present
- High dependency unit: HDU is a clinically specified area where the facility for continuous monitoring of vital signs is present and the staffing ratio is in between ward and ICUs
- General ward: A General ward is a place where patients with a variety of conditions and varying degrees of severity are managed. There is a variable staffing pattern in various hospitals but it is not as intensive as HDUs and ICUs.

As one does not require sedation and paralysis for NIV, it is possible to apply this modality outside the ICU. It is expected that the application of NIV outside the ICU will ease the pressure on ICU beds. Randomized controlled trials have proved the effectiveness of NIV in both ICU and wards.[19] One must remember that these studies were done in units committed to ventilation by noninvasive approach and with required expertise. This factor, more than any other, has been important in determining the outcome.

The outcome of NIV is remarkably similar in different settings viz. research institutes and peripheral usual care providers.[184] Studies have shown that regardless of the location, the success of NIV is similar between community teaching hospitals and ICUs across Europe. When a well-trained staff is available, it really does not matter. There are only a few prospective randomized controlled studies of NIV outside the ICU.[13,25,27] these studies lacked the number, which precluded conclusive inferences. However, in a large study[19] covering 13 centers (n = 236), NIV was applied in the general wards by the usual ward staff, using a bilevel device in spontaneous mode, following a simple protocol. The study showed that with NIV treatment failures could be reduced from 27 to 15% ($P < 0.05$) and mortality in these patients reduced from 20 to 10% ($P < 0.05$). In patients with pH <7.3, results of initial treatment in the ward was inferior to that of patients treated in the ICUs. It was also demonstrated that early NIV in a general ward resulted in a better outcome than providing no ventilatory support for acidotic patients outside the ICUs. However most of the patients studied were those with acute exacerbation of COPD. The results thus indicated that NIV could be applied with benefit outside the ICU by trained usual ward staff and early introduction of NIV in a general ward results in a better patient outcome.

There are no RCTs of NIV outside ICUs in patients with hypoxemic respiratory failure or for weaning. Currently, some data is available from the study of Antonelli *et al*.[65]

Although, theoretically NIV can be applied in the Emergency Department (ED), in India the distinction between ED and ICU fades away in many hospitals. Most patients with an acute exacerbation of COPD coming to ED do not actually need NIV. Those patients who remain acidotic and tachypnoeic after a while after starting standard medication should be put on NIV in the ED. However, it is imperative that staff trained to initiate and monitor NIV is available in the ED. CPAP has been shown to be of benefit in acute cardiogenic pulmonary edema.[68,70] in the emergency department. The time spent in emergency ward will vary from hospital to hospital. In some hospitals as soon as the patient is stabilized and bed is arranged, he is shifted to the ward. Others have observation facilities for few hours. NIV can be started in the emergency ward and the patient quickly transferred to a place where mask expertise is available.

Success of NIV depends on the initial evaluation and/or the response to a short-term trial. This obviously depends upon the skill of the staff and basic minimal monitoring of parameters to detect early failure. The first few hours are of vital importance and it is mandatory to monitor parameters (SpO_2, arterial Blood Gases, vital signs, patient comfort, mask leaks and the patient's ability to expectorate) by trained personnel, be it a nurse, respiratory therapist or a physician. There is not much information especially in randomized clinical trials in the literature on 'who' should perform NIV. In fact many of the guidelines published have taken for granted the automatic and universal existence of respiratory therapists. In a country like India respiratory therapists are scarce and nurses are not trained in NIV. So for some time to come, it will be the physicians who will take primary responsibility of initiating and monitoring NIV.

It is important that the attending staff be able to detect the non-responding patient by frequent clinical examination and persistently abnormal blood gases. They should also be familiar with the equipment, explanation of the procedure to the patient and potential complications of NIV. Nurses, physiotherapists or respiratory therapists may be the caregivers and this will also depend on local availability and enthusiasm and expertise.

If a patient has pH <7.3, they are better managed in HDU or ICU.

Recommendations

- In acute respiratory failure, NIV can be provided in many locations in the hospital like in ICU, high dependency area, respiratory ward or NIV unit, emergency ward or general ward. However, in India for the time being ICU is the best place. (Level III)
  Choosing a location for NIV will depend on many factors like clinical state of the patient, severity of respiratory failure, significant co-morbidity and the condition for which NIV is being applied. This will also depend on whether the patient will be intubated if NIV fails, patient's nursing requirements and skill level of the physician, experienced nurse and therapist.(Level II)
- A trained person who could be a physician, physiotherapist or a house nursing staff can initiate NIV. The outcome will depend on the training of the individual. Minimal mandatory requirements of the staff should include the ability to monitor the NIV trial, vital parameters (such as saO_2, $paCO_2$, pH, vital signs, patient comfort, mask leaks, patient's ability

to handle secretions etc) and more importantly to recognize failure of NIV. (Level III)

- A ward with trained staff will show a better outcome than an ICU with high nurse doctor ratio and high level of monitoring but little experience of NIV. (Level III)
- Patient who require continuous NIV and cannot sustain oxygenation during even a brief discontinuation are better managed in ICU or HDU. (Level III)
- There must be a proper protocol of who will start and who will monitor the patient and at what frequency the ABG will be sent. (Level III)
- Any area, which has the following facilities, can be used for applying NIV: (Level II)
- Staff with training and expertise in NIV on a 24 hr basis
  - Rapid access to endotracheal intubation and invasive mechanical ventilation
  - Facilities for monitoring
  - Oximetry
  - Frequent monitoring by staff nurse and documentation.
- NIV should be applied in the ward on only those patients who are suffering from a disease state where the role of NIV has been established. (Level III)
- Patient who fulfills the following criteria can be ventilated in the wards:
  - COPD patients (pH >7.30), who are not seriously ill
  - Patients who can protect their airways
  - Requirement of intubation appears unlikely.

Trained staff nurse should be available to monitor patient frequently. It is also essential to have good nurse to patient ratio with a minimum of one to four in the ward.

- Patients who fulfill the following criteria can be ventilated in HDU and emergency ward.
  - Patient who can tolerate brief discontinuation of NIV mask.
  - Patient suffering from COPD, cardiogenic pulmonary edema, acute respiratory failure in obstructive sleep apnea and mild cases of hypoxemic respiratory failure.
  - PH <7.3 but more than 7.2.

In addition to trained staff to monitor NIV, intubation equipment should also be available in the same area.

Those patients who have a greater likelihood of failure should always be ventilated in the ICU i.e., pneumonia, ARDS and asthma.

Starting NIV service (158)

NIV services can be started if the following conditions are fulfilled.

- Availability of necessary equipment. A simple pressure targeted machine would be ideal
- There should be supply of range of nasal, facemasks and tubes
- Facility for cleaning and disinfecting mask and tubing should be available
- Trained staff with basic knowledge of NIV, masks and ventilatory circuit should be available. They should know how to adjust setting, how to manage leaks and minor problems including cleaning and disinfecting
- Nurses with previous experience in the ICU/NIV are useful
- One physician trained in NIV should be available on call 24 hours a day.

Management of COPD with limited resources

COPD, the 12th most common disease worldwide, is a major cause of mortality and morbidity. The 2002 WHO world health report lists it as the fifth leading cause of death in the world.[181] It is expected that by 2020, COPD will become the third most common cause of death.[182] The burden of COPD is high in developing countries. The morbidity data greatly underestimates the true prevalence of the disease due to under reporting. The median values of prevalence rates of COPD in India have been estimated to be 5% in males and 2.7% in females.[183]. In 1996 the total number of adult patients more than 30 years of age was estimated to be 8.16 million males and 4.21 million femalesThe comparatively higher prevalence rates of COPD in women in developing countries is due to a high exposure to indoor particulate air pollution caused by cooking with biomass fuels in poorly ventilated dwellings. Thus we face a large, often underestimated, burden of COPD, which is predicted to assume epidemic proportions in the next decade.

Patients with COPD are prone to exacerbations as their disease progresses. Exacerbations in COPD are associated with significant morbidity and mortality. In a large study, Connors and colleagues studied more than 1000 patients admitted to hospital with severe hypercapnic exacerbations of COPD. Half of these patients had to be admitted to the ICU, with 35% of them needing mechanical ventilation. Hospital mortality was 11%.[184] Seneff *et al.* have also demonstrated a high in-hospital mortality of 24% in COPD patients admitted to the ICU.[185]

In our country, a large number of patients with COPD die due to a lack of management facilities when they present in acute exacerbations with hypercapnic respiratory failure. These patients cannot on most occasions be shifted to a well equipped centre as facilities for invasive ventilation are few and the numbers of ICU beds are far less than needed. There is, therefore, a pressing need for simple, inexpensive but effective therapeutic interventions for treating critically ill patients even in centers where ICUs are not available.

NIV reduces the need for intubation, risk of treatment failure, length of hospital stay and mortality in these patients. Although earlier studies of NIV in COPD patients have been reported in an ICU setting, there is now enough evidence that NIV can be initiated even in general wards with simple ventilators. In a landmark prospective multicentric study in patients of COPD in 14 centers in UK, Plant *et al*.[128] demonstrated that the need for intubation was reduced from 27 to 15% by NIV in general wards and hospital mortality was reduced from 20 to 10%. The ward staff with little or no previous experience was able to administer NIV after training. NIV was administered with an unsophisticated ventilator and only the levels of inspiratory and expiratory pressures were adjusted according to a simple protocol. This study of ward based NIV for acute exacerbations of COPD confirmed that it is a highly cost-effective treatment. This data suggests that non-invasive ventilation in wards can avoid admissions to intensive care units and reduce both costs and deaths, especially in developing countries.

In a survey of NIV in patients with acute exacerbations of COPD in UK, about 20% centers used clinical guidelines without ABG to select patients for treatment with NIV, These included exhaustion and failure to improve on standard treatment.[186] In another study, Plant *et al.* have estimated that 46.7% patients admitted to a district general hospital in UK were hypercapnic and 20% had respiratory acidosis (pH < 7.35).[187] There was however a consensus in the panel that the number of patients deserving treatment in our country is large with a wide demand supply gap.

The skills required for NIV are easily learnt and the equipment required is relatively inexpensive. The complication rate is very low when compared to invasive ventilation. Physicians and nurses can use NIV early outside the ICU to prevent deterioration in the patient's condition as NIV can be started at an early stage in the evolution of respiratory failure. Reversing respiratory failure is likely to be easier at an early stage when, theoretically, lower pressures used for shorter periods may improve the physiological disturbances.

NIV in general wards thus appears to be a suitable treatment modality for low-income countries because of the limited availability of ICU facilities. The expert panel therefore believes that there is evidence to support the use of NIV in acute exacerbations of COPD even in smaller centers without ICU facilities.

Another significant question raised by some members and the international reviewer was whether or not NIV can be administered in selected COPD patients with acute exacerbations in the absence of facility for ABG. Equipment for NIV and oxymetry is much easier to install and maintain than a blood gas testing facility. The expert panel believes that this simple and inexpensive modality should be tried in selected patients even in the absence of blood gas testing facility or ICU, if well trained staff is available. At present such patients get only medical treatment and many of them die due to unavailability of any ventilatory support. Of course it may lead to overuse of NIV but it will save many lives.

Recommendations

- "NIV can be used if the arterial blood gases report of a patient with acute exacerbation of COPD shows a pH <7.35 with a $paCO_2$ >45 mm Hg, even if facilities for invasive ventilation are not available" (level III)
- The expert panel recommends that in acute exacerbations of COPD, NIV can be used even if no facilities for ABG testing or ICU are available in the following circumstances: (Level III)
  - Failure of exacerbation to respond to initial medical management with increasing dyspnea
  - Use of accessory muscles with paradoxical chest and abdominal movements or onset of new physical signs-cyanosis, peripheral edema or mild confusion, lethargy or alteration in sensorium
  - Appearance of signs of hypercapnia-peripheral venous dilatation, tachycardia despite optimal oxygen saturation, bounding pulse with wide pulse pressure, asterixis (flaps), throbbing headaches
  - Persistent or worsening hypoxemia despite supplemental oxygen
  - Significant co-morbid disease-cardiac, uncontrolled diabetes etc.
- The expert panel recommends that facilities for NIV with adequately trained staff should be made available for treating patients with COPD at all levels of care-primary health centers, small nursing homes in towns, secondary care (district level hospitals, large multispeciality nursing homes in cities) and tertiary care level (medical colleges, corporate and specialty hospitals. (Level III)
- In circumstances of NIV application in the absence

of ABG facilities or invasive ventilatory support and ICU care physicians must educate themselves on the signs of failure of NIV support and refer patients to a higher level of care if feasible after 4 hours of trial. (Level III)

Practice points

In addition to trained staff, the following minimum equipment should be available before NIV service can be initiated:

- Pulse oxymetry
- Portable pressure ventilator
- Adequate supply of oxygen
- ECG monitoring.

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