

ISCCM Guidelines for the Use of Non-invasive Ventilation in Acute Respiratory Failure in Adult ICUs

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ABSTRACT

A. ACUTE HYPERCAPNIC RESPIRATORY FAILURE

A1. Acute Exacerbation of COPD: Recommendations: NIV should be used in management of acute exacerbation of COPD in patients with acute or acute-on-chronic respiratory acidosis (pH = 7.25-7.35). (1A) NIV should be attempted in patients with acute exacerbation of COPD (pH <7.25 & PaCO₂ ≥ 45) before initiating invasive mechanical ventilation (IMV) except in patients requiring immediate intubation. (2A). Lower the pH higher the chance of failure of NIV. (2B) NIV should not be used routinely in normo- or mildly hyper-capnic patients with acute exacerbation of COPD, without acidosis (pH > 7.35). (2B) **A2. NIV in ARF due to Chest wall deformities/ Neuromuscular diseases:** Recommendations: NIV may be used in patients of ARF due to chest wall deformity/Neuromuscular diseases. (PaCO₂ ≥ 45) (UPP) **A3. NIV in ARF due to Obesity hypoventilation syndrome (OHS):** Recommendations: NIV may be used in AHRF in OHS patients when they present with acute hypercapnic or acute on chronic respiratory failure (pH 45). (3B) NIV/CPAP may be used in obese, hypercapnic patients with OHS and/or right heart failure in the absence of acidosis. (UPP) **B. NIV IN ACUTE HYPOXEMIC RESPIRATORY FAILURE:**

B1. NIV in Acute Cardiogenic Pulmonary Oedema: Recommendations: NIV is recommended in hospital patients with ARF, due to Cardiogenic pulmonary edema. (1A). NIV should be used in patients with acute heart failure/ cardiogenic pulmonary edema, right from emergency department itself. (1B) Both CPAP and BiPAP modes are safe and effective in patients with cardiogenic pulmonary edema. (1A). However, BPAP (NIV-PS) should be preferred in cardiogenic pulmonary edema with hypercapnia. (3A) **B2. NIV in acute hypoxemic respiratory failure:** Recommendations: NIV may be used over conventional oxygen therapy in mild early acute hypoxemic respiratory failure (P/F ratio <300 and >200 mmHg), under close supervision. (2B) We strongly recommend against a trial of NIV in patients with acute hypoxemic failure with P/F ratio <150. (2A) **B3. NIV in ARF due to Chest Trauma:** Recommendations: NIV may be used in traumatic flail chest along with adequate pain relief. (3B) **B4. NIV in Immunocompromised Host:** Recommendations: In Immunocompromised patients with early ARF, we may consider NIV over conventional oxygen. (2B). **B5. NIV in Palliative Care:** Recommendations: We strongly recommend use of NIV for reducing dyspnea in palliative care setting. (2A) **B6. NIV in post-operative cases:** Recommendations: NIV should be used in patients with post-operative acute respiratory failure. (2A) **B6a. NIV in abdominal surgery:** Recommendations: NIV may be used in patients with ARF following abdominal surgeries. (2A) **B6b. NIV in bariatric surgery:** Recommendations: NIV may be used in post-bariatric surgery patients with pre-existent OSA or OHS. (3A) **B6c. NIV in Thoracic surgery:** Recommendations: In cardiothoracic surgeries, use of NIV is recommended post operatively for acute respiratory failure to improve oxygenation and reduce chance of reintubation. (2A) NIV should not be used in patients undergoing esophageal surgery. (UPP) **B6d. NIV in post lung transplant:** Recommendations: NIV may be used for shortening weaning time and to avoid re-intubation following lung transplantation. (2B) **B7. NIV during Procedures (ETI/Bronchoscopy/TEE/Endoscopy):** Recommendations: NIV may be used for pre-oxygenation before intubation. (2B) NIV with appropriate interface may be used in patients of ARF during Bronchoscopy/Endoscopy to improve oxygenation. (3B) **B8. NIV in Viral Pneumonitis ARDS:** Recommendations: NIV cannot be considered as a treatment of choice for patients with acute respiratory failure with H1N1 pneumonia. However, it may be reasonable to use NIV in selected patients with single organ involvement, in a strictly controlled environment with close monitoring. (2B) **B9. NIV and Acute exacerbation of Pulmonary Tuberculosis:** Recommendations: Careful use of NIV in patients with acute Tuberculosis may be considered, with effective infection control precautions to prevent air-borne transmission. (3B) **B10. NIV after planned extubation in high risk patients:** Recommendation: We recommend that NIV may be used to wean high risk patients from invasive mechanical ventilation as it reduces re-intubation rate. (2B) **B11. NIV for respiratory distress post extubation:** Recommendations: We recommend that NIV therapy should not be used to manage respiratory distress post-extubation in high risk patients. (2B) **C. APPLICATION OF NIV:** Recommendation: Choice of mode should be mainly decided by factors like disease etiology and severity, the breathing effort by the patient and the operator familiarity and experience. (UPP) We suggest using flow trigger over pressure triggering in assisted modes, as it provides better patient ventilator synchrony. Especially in COPD patients, flow triggering has been found to benefit auto PEEP. (3B) **D. MANAGEMENT OF PATIENT ON NIV:**

D1. Sedation: Recommendations: A non-pharmacological approach to calm the patient (Reassuring the patient, proper environment) should always be tried before administrating sedatives. (UPP) In patients on NIV, sedation may be used with extremely close monitoring and only in an ICU setting with lookout for signs of NIV failure. (UPP) **E. EQUIPMENT:** Recommendations: We recommend that portable bilevel ventilators or specifically designed ICU ventilators with non-invasive mode should be used for delivering Non-invasive ventilation in critically ill patients. (UPP) Both critical care ventilators with leak compensation and bi-level ventilators have been equally effective in decreasing the WOB, RR, and PaCO₂. (3B) Currently, Oronasal mask is the most preferred interface for non-invasive ventilation for acute respiratory failure. (3B) **F. WEANING:** Recommendations: We recommend that weaning from NIV may be done by a standardized protocol driven approach of the unit. (2B)

Keywords: Acute respiratory failure, Chronic obstructive pulmonary disease, Guidelines, ICU, Mechanical ventilation, Non invasive ventilation.

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INTRODUCTION

The term non-invasive ventilation (NIV) refers to the application of ventilation without any conduit access to the airways i.e, without an endotracheal or tracheostomy tube.¹ NIV has been used for over 25 years for the treatment of respiratory failure with indications for its use ever expanding and list of contraindications decreasing.²⁻⁸ Use of NIV leads to avoidance of endotracheal intubation (ETI). Hence, it decreases the incidence of ETI-associated complications like hospital acquired pneumonia (26%) and sinusitis (7- 40%).⁹⁻¹⁵ The Indian Society of Critical Medicine published NIV guidelines few years ago which needed to be updated in view of the availability of more evidence.^{1,8}

MATERIALS AND METHODS

This document is an expert consensus based guidelines for the use of NIV in the management of acute respiratory failure (ARF) in various disease states based on the available current literature. A systemic search was performed of MEDLINE, PUBMED and EMBASE databases using the search terms NIV, NIMV, NIPPV and disease name. We limited our search to English articles. The articles were divided into RCTs, systemic reviews, meta-analysis, case series and case reports. The expert group meeting was convened under the aegis of Indian Society of Critical Care Medicine at Pune. The expert group included intensivists from all over India. The evidence on each question was presented and deliberated. Recommendations were formulated and graded according to previous evidence based guidelines of ISCCM¹⁶ (Table 1). When there was no evidence, the recommendations were named as Useful Practice Point (UPP)

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INDICATIONS FOR USING NIV

The indications for the use of NIV have come to encompass a large and diverse number of clinical situations (Table 2).

ACUTE HYPERCAPNIC RESPIRATORY FAILURE NIV in Acute Exacerbation of COPD

Almost a quarter of COPD patients who come to hospital develop ARF over the course of their hospitalization.^{17,18} The presence of ARF is an independent risk factor for death in these patients.¹⁹ NIV has been used in COPD for more than two decades and has both preventive and therapeutic implications.²⁰⁻⁴⁶ There are numerous, randomized controlled trials, meta-analyses and case series conducted in these patients, which have demonstrated the efficacy of NIV in acute exacerbation of COPD.

NIV has been used in these patients i) to prevent the development of acute respiratory acidosis (Patients with normal or raised PaCO₂, Normal pH) or ii) to prevent use of invasive mechanical

Table 1: Criteria for quality of evidence levels and grading of strength of recommendations used in formulation of current guidelines

Quality of Evidence	Level
Evidence from ≥ 1 good quality and well conducted randomized control trial(s) or meta-analysis of RCT's	1
Evidence from at least 1 RCT of moderate quality, or well-designed clinical trial without randomization; or from cohort or case-controlled studies.	2
Evidence from descriptive studies, or reports of expert committees, or opinion of respected authorities based on clinical experience	3
Not backed by sufficient evidence; however, a consensus reached by the working group, based on clinical experience and expertise	(UPP)
Strength of Recommendations	Grade
Strong Recommendations to do (or not to do) where the benefits clearly outweigh the risk (or vice versa) for most, if not all patients	A
Weak Recommendations, where benefits and risk are more closely balanced or are more uncertain	B

UPP, useful practice point; RCT, randomized controlled trial

Table 2: Indication of NIV in Acute Respiratory Failure

Sr. No.	Acute Hypercapnic Respiratory Failure	Acute Hypoxemic Respiratory Failure	Special Conditions
1.	Acute exacerbation of Chronic Obstructive Pulmonary disease	Acute Cardiogenic Pulmonary Edema	Post-Extubation
2.	Acute Asthma	ARDS	Weaning in progress
3.	Acute Exacerbation of Bronchiectasis	Pneumonia	Pre/Post Operative
4.	Acute Decompensation in Obesity Hypoventilation Syndrome	Multifactorial ARF in Immunocompromised patients	Palliative or Comfort Care
5.	Acute Decompensation in Neuromuscular Disease		Chest Trauma
6.	Chest wall deformity		NIV during procedures

ventilation (IMV) [mild to moderate Acute respiratory acidosis (pH 7.25- 7.35) + respiratory distress (PaCO₂>45)], and iii) therapeutically as an alternative to IMV in patients having severe acidosis (pH<7.25) and very severe respiratory distress. NIV should be used in these patients in addition to standard medical therapy.²⁻⁸

In a review of 17 RCTs involving a total of 1264 patients of AECOPD with ARF, Osadnik et al, reported that NIV decreased i) the risk of mortality (by almost half), ii) need for invasive mechanical ventilation (IMV) following endotracheal intubation (ETI) (by 65%), iii) Length of Stay (LOS) in hospital (by almost 3 and half days), iv) incidence of complications (other than those related to NIV).⁴⁴ Use of NIV also lead to improvement in biochemical parameters within an hour- increase in pH (by 0.05) and Oxygenation (by 7.47 mmHg) and a reduction in Carbon dioxide (by 4.62 mmHg).⁴⁴ Keenan et al performed a meta-analysis of 15 RCTs in patients with AECOPD with ARF of varying severity. NIV reduced the need for IMV (in almost 30% of patients), hospital LOS (by 4 and half days) and mortality (by 10%).⁴⁷

NIV in AECOPD with Acute hypercapnic respiratory failure and acidosis (pH 7.25-7.35) to prevent ETI and IMV

Use of NIV in this clinical setting has been demonstrated to have maximum beneficial effect.²⁰⁻⁴⁵ There is improvement in both pH as well as breathing, usually within an hour.⁴⁸ NIV improves clinical sense of well-being in patients and mortality rates, reduces rates of ETI/ respiratory and non-respiratory infections and reduces hospital and ICU LOS.⁴⁹⁻⁵⁰

NIV in AECOPD with ARF with no or very mild acidosis

In an analysis of the subgroup of patients with mild exacerbation of AECOPD with ARF (PaCO₂ ≥45 mmHg, pH> 7.35), Keenan et al demonstrated that the use of NIV was not beneficial.⁴⁷ A subsequent RCT conducted by Keenan et al, in 52 patients with AECOPD without acidosis, comparing use of NIV plus standard therapy versus standard treatment alone showed poor tolerance of NIV and no benefit of use of NIV (no improvement in mortality on using IMV).²⁰ In a previous small study (24 patients) on use of NIV in COPD patients with mild exacerbations (none of the patients required IMV or died), Barbe et al found no improvement in the Borg dyspnea score in patients who were given NIV. 30% of patients did not tolerate NIV.²¹ Another RCT as well as an observational study showed similar findings (poor intolerance and no benefit in terms of mortality or use of IMV in patients with AECOPD and mild or no acidosis).^{22,23}

NIV in AECOPD with Acute hypercapnic respiratory failure with severe acidosis (pH<7.20)

These patients usually require immediate ETI and IMV. Conti et al demonstrated that NIV was superior to IMV even in this setting.³³ Patients who were ventilated noninvasively had lesser ICU and hospital LOS, infections and other complications. But there was no benefit in terms of survival. Both set of patients (ventilated invasively or non-invasively) demonstrated a similar mortality rate. Another RCT also demonstrated similar results. IMV was beneficial in rapid improvement in sensorium but had longer duration of ventilator use and ICU LOS.³⁶ NIV was associated with fewer respiratory infections and tracheostomies. There was no difference in mortality rates in the two set of patients.³⁶

Some patients require immediate ETI and IMV and NIV should not be implemented in these patients, e.g. - respiratory arrest, delirium requiring sedation, bradycardia (HR< 60 per minute) and hypotension (MAP <60 mmHg).³³ NIV is not contraindicated in patients with coma due to high CO₂ levels. In a large case series,

Diaz et al showed that NIV can be used in hypercapnic comatose patients with AECOPD.⁵¹

Recommendations

NIV should be used in the management of acute exacerbation of COPD in patients with acute or acute-on-chronic respiratory acidosis (pH = 7.25-7.35). (1A)

NIV should be attempted in patients with acute exacerbation of COPD (pH <7.25 & PaCO₂ ≥ 45) before initiating invasive mechanical ventilation (IMV) except in patients requiring immediate intubation (2A). Lower the pH, higher the chance of failure of NIV. (2B)

NIV should not be used routinely in normo- or mildly hypercapnic patients with acute exacerbation of COPD, without acidosis (pH > 7.35). (2B)

NIV in ARF due to Chest wall deformities/Neuromuscular diseases

There are no RCTs which compare NIV and IMV in these patients subsets. There are few studies with a small number of patients.⁵²⁻⁵⁴ Patients with kyphoscoliosis and neuromuscular diseases who present with Acute hypercapnic respiratory failure benefit from the use of NIV. There is improvement in gas exchange and ETI may be avoided.

Recommendations

NIV may be used in patients of ARF due to chest wall deformity/ Neuromuscular diseases. (PaCO₂ ≥ 45) (UPP)

NIV in ARF due to Obesity hypoventilation syndrome (OHS)

NIV (Bilevel) or CPAP have both been used in patients with OHS and acute or chronic respiratory failure.⁵⁵⁻⁵⁶ Patients with OHS and ARF present with acidosis should be treated with bilevel NIV. There are no RCTs on the use of NIV/CPAP in these patients. Carillo et al prospectively studied the application of NIV in 173 patients with OHS and 543 patients with COPD.⁴⁵ They found that patients with OHS and ARF could be managed with NIV as effectively and with better outcomes than COPD patients managed with a similar NIV protocol.

Recommendations

NIV may be used in Acute Hypercapnic Respiratory Failure (AHRF) in OHS patients when they present with acute hypercapnic or acute on chronic respiratory failure (pH <7.35 & PaCO₂ >45). (3B)

NIV/CPAP may be used in obese, hypercapnic patients with OHS and/or right heart failure in the absence of acidosis. (UPP)

NIV in Acute Hypoxemic Respiratory Failure

NIV in Acute Cardiogenic Pulmonary Oedema

The benefit of NIV in acute cardiogenic pulmonary edema (ACPE), was first described in 1930 by Barach and Poulton.^{57,58} Currently, the use of NIV has increased in pre-hospital, emergency room and ICU settings. Many randomised trials have evaluated the effectiveness of NIV in ACPE, and have found significant improvement in physiological parameters like (heart rate, RR, BP), and also cardiopulmonary indices (SV, CO, CI, PCWP).⁵⁹ However, none have shown a mortality benefit. The 3CPO trial is the largest multi-center, prospective randomized trial of use of NIV in ACPE;

with 1069 patients.⁶⁰ The trial demonstrated no difference in 7-day mortality, with the use of CPAP, BPAP or oxygen. However, use of NIV was shown to improve breathlessness, HR and acidosis.

A systemic review of 15 randomized controlled trials from 10 countries and 727 patients, showed significant reduction in in-hospital mortality and intubation with use of NIV in ACPE.⁶¹ The use of CPAP found a statistically significant reduction in in-hospital mortality, whereas use of BPAP led to a non-significant reduction in the same. There was no difference in outcomes with the use of CPAP or BPAP (included 219 patients). Another meta-analysis of 23 RCTs also demonstrated similar findings.⁶²

A Cochrane database, of 2916 patients with ACPE, from 32 RCTs, showed significant reduced hospital mortality and intubation rates with use of NIV.⁶³ In a multicentre prospective observational study, ACPE SIMEU study group found NIV to have high clinical effectiveness in treatment of ARF due to ACPE as compared to conventional O₂ therapy.⁶⁴

Recommendations

NIV is recommended in hospital patients with ARF, due to Cardiogenic pulmonary edema. (1A)

NIV should be used in patients with acute decompensated heart failure/ cardiogenic pulmonary edema, right from emergency department itself. (1B)

CPAP and BPAP are the two principal modes used in ACPE. Agarwal et al combined the data of all RCTs of CPAP vs BPAP in ACPE, and found that BPAP increased intubation rates, and probably hospital mortality.⁶⁵ However, it was not statistically significant, and they concluded that more studies were needed to compare. When CPAP and BPAP were compared in the systemic review by Vital and Colleagues, CPAP had better efficacy, safety and cost effectiveness as compared to BPAP and was to be preferred in this situation.⁶³

Recommendations

Both CPAP and BiPAP modes are safe and effective in patients with cardiogenic pulmonary edema. (1A)

However, BPAP (NIV-PS) should be preferred in cardiogenic pulmonary edema with hypercapnia. (3A)

Among the newer modes available, not much research is available to recommend their use in ACPE. In patients with ACPE, rapid introduction of Adaptive Support Ventilation (ASV) in the Emergency Room reduced the rate of intubation.⁶⁶ Proportional Assist Ventilation (PAV) was also not found to be superior to CPAP with regard to tolerance and efficacy.⁶⁷

NIV in acute hypoxemic respiratory failure

Initial studies failed to show any added benefit of NIV in ARDS, despite physiological rationale available with its use.⁶⁸ However, by the end of the decade, a meta-analysis of 13 studies and 540 subjects, showed that use of NIV in ARDS was associated with 48% intubation rates, and thus, 50% patients benefitted without needing intubation.⁶⁹ Further more studies proved this point.^{70,71} In 2013, an observational cohort study of 113 patients showed an intubation rate of 35% in non-ARDS hypoxemic respiratory failure and in mild ARDS. However, in patients with severe hypoxemia, (PaO₂/FiO₂ <150) 84% of the patients required intubation.⁷⁰ These findings were supported by another observational study, which concluded that NIV is safe in mild ARDS. However, in moderate to severe ARDS, it

should be used with caution.⁷¹ Also; additional factors like shock, high APACHE II scores, and low PAO₂/FiO₂ scores were associated with risk of NIV failure and mortality.

In a meta-analysis of 2017, including 11 randomised studies and 1480 patients of acute hypoxemic nonhypercapnic failure of varied etiology showed that the use of NIV significantly reduced intubation rates and hospital mortality.⁷² Subgroup analysis showed an advantage of helmet (as compared to face or nasal mask) and BPAP, (over the other modes) in reducing the ICU mortality. In the Lung Safe study, patients of ARDS with lower ratio of PaO₂ to inspired oxygen (P/F) less than 150mmHg, had been found to be associated with higher chances of NIV failure and increased mortality (36.2% in NIV group vs 24.7% in invasive ventilation group).⁷³

Bellani et al recently found that the use of NIV in moderate to severe ARDS may be associated with a worse ICU outcome than invasive mechanical ventilation.⁷⁴ While mortality rate was low for patients who were successfully managed with NIV, patients who failed NIV had a high mortality. A recent pilot multicentre RCT of 200 subjects with pneumonia induced early mild ARDS; NIV did not appear to help in reducing the number of intubations, despite the improvement in the PaO₂/FiO₂ ratio after 2 hours of NIV use.⁷⁵

Recommendations

NIV may be used over conventional oxygen therapy in mild early acute hypoxemic respiratory failure (P/F ratio < 300 and > 200 mmHg), under close supervision. (2B)

We strongly recommend against a trial of NIV in patients with acute hypoxemic failure with P/F ratio < 150. (2A)

NIV in ARF due to Chest Trauma

There are 3 RCTs which deal with the use of NIV in patients with ARF due to chest trauma.⁷⁶⁻⁷⁸ These RCTs show evidence from a small number of patients (total 171 patient in the 3 RCTs). NIV when used in patients with chest trauma is beneficial (reduced infectious complications and ICU and hospital stay) when compared with use of high flow oxygen through a mask or ETI and invasive MV.⁷⁶⁻⁷⁸ Therefore, the British Thoracic Society guidelines gave low grade recommendations for the use of non-invasive ventilation in trauma patients.² The Canadian Critical Care Trials Group/Canadian Critical Care Society Non-invasive Ventilation Guidelines Group gave no recommendation for use of NIV in patients with chest trauma, due to lack of sufficient evidence.⁷⁹

Recommendations

NIV may be used in traumatic flail chest along with adequate pain relief. (3B)

NIV in Immunocompromised Host

In 2001, a prospective randomised trial of 52 immunosuppressed patients with pneumonitis, fever and early hypoxemic respiratory failure, showed a significant reduction in intubation rates and improved likelihood of survival to hospital discharge, in patients with NIV.⁸⁰ In a large retrospective cohort study of use of NIV for acute hypoxemic respiratory failure in 1614 cancer patients, concluded NIV failure as an independent risk factor for ICU mortality.⁸¹

A recent post hoc analysis, of Lung Safe study, revealed the tendency of increased NIV use in the immunocompromised host,

and patients with NIV, had a 48% rate of intubation.⁸² However, then there were trials with conflicting results. In a multicentre randomised trial of 374 immunocompromised subjects, early NIV, compared with standard oxygen, was not associated with clinical benefits in mortality, ICU-acquired infections, duration of mechanical ventilation or length of ICU stay.⁸³ Similarly, The Efraim multinational prospective cohort study of immunocompromised patients with acute hypoxemic respiratory failure, the initial choice of oxygenation and ventilation strategy (standard oxygen vs High Flow Nasal Cannula (HFNC) vs NIV vs NIV + HFNC) did not affect mortality.⁸⁴

A meta-analysis published in 2017 by Huang et al showed that early use of NIV is effective in reducing short term mortality in selected immunocompromised patients with acute respiratory failure.⁸⁵ A recent meta-analysis of RCTs by Zayed et al showed that use of NIV in immunocompromised with acute hypoxemic respiratory failure, was associated with a significant reduction in the rate of intubations. However, no significant difference in mortality or ICU acquired weakness was seen.⁸⁶ A meta-analysis comparing invasive and non-invasive ventilation in immunocompromised patients, showed more benefits with use of NIV, with a significant reduction in in-hospital mortality and 30-day mortality.⁸⁷

Recommendation

In Immunocompromised patients with early ARF, we may consider NIV over conventional oxygen. (2B)

NIV in Palliative Care

In a randomised feasibility trial, Nava and colleagues recruited 200 patients with solid tumours and acute respiratory failure and limited life expectancy. The study showed a clear decrease in Borg dyspnoea score in the NIV group, along with lower requirement of total dose of morphine in the first 48 hrs. Adverse events leading to NIV discontinuation were mainly related to mask intolerance and anxiety.⁸⁸

Recommendation

We recommend use of NIV for reducing dyspnea in palliative care setting. (2A)

NIV in post-operative cases

Post-operative respiratory failure due to any surgery is a result of anaesthesia, postoperative pain, and diaphragmatic dysfunction associated with both thoracic and abdominal surgeries. Hypoxemic respiratory failure is a result of lung volume reduction and atelectasis while hypercapnic respiratory failure is due to muscle fatigue.⁸⁹ Both CPAP or bilevel NPPV plays an important role in the post-operative period. NIV prevents further intubation, shortens time on mechanical ventilation, prevents nosocomial infections, and significant morbidity and mortality after surgery.

Recommendations

NIV should be used in patients with post-operative acute respiratory failure. (2A)

NIV in abdominal surgery

A multicentre RCT published by Jaber et al included 298 patients with hypoxemic respiratory failure post abdominal surgery. It

compared use of NIV versus standard oxygen therapy. NIV reduced risk of ventilator associated pneumonia (31% versus 49%; P= 0.003) and reduced risk of reintubation within 7 days (46% versus 33%; p= 0.03).⁹⁰ In another prospective observational study, Jaber et al showed that NIV use in this situation avoided reintubation in 67% and improved mortality by reducing hospital stay.⁹¹ Ferreyra et al in their meta-analysis of 9 RCTs found that CPAP reduced pulmonary complications (atelectasis, pneumonia) in patients undergoing abdominal surgery.⁹²

Recommendations

NIV may be used in patients with ARF following abdominal surgeries. (2A)

Role of NIV in bariatric surgery

Obesity is a significant risk factor for developing obstructive sleep apnoea (OSA). Approximately 27 to 70 % of patients undergoing bariatric surgery show co-existence of OSA.⁹³⁻⁹⁵ Kaw et al explained that patients with obesity hypoventilation syndrome with or without OSA are more likely to develop post-operative complications including respiratory failure. There was a resultant increase in the use of NIV in post-operative condition to overcome OSA or OHS.

Both Gaszynski et al and Pessoa et al have shown that non-invasive ventilation improves oxygenation in postoperative obese patients.^{96,97} Wong et al compared the use of the CPAP mask with the standard air-entrainment mask and found improving oxygenation but no difference in postoperative %FEV1 and %FVC.⁹⁸

In a large observational study of more than 5,000 patients with OSA and planned for bariatric surgery conducted by Stefan et al found that one out of five patients received NIV on the day of or the day after surgery.⁹⁹ Early use of NIV in post-operative period did not improve outcomes, including chances of reintubation, mortality and hospital length of stay. Two single-centre retrospective cohort studies, one of patients undergoing Roux-en-Y bypass and the other of patients undergoing gastric banding surgeries, did not show any benefit of NIV in post-operative period.^{100,101} Systemic review of literature by Tong S et al found no increased anastomotic dehiscence risk when NIV is administered during immediate post-bariatric surgery.¹⁰²

Recommendations

NIV may be used in post-bariatric surgery patients with pre-existent OSA or OHS. (3A)

Role of NIV in Thoracic surgery

In cardiothoracic surgeries deterioration of pulmonary function is a frequent postoperative complication and remains a significant cause of postoperative mortality.¹⁰³ Impaired oxygenation is primarily attributed to a decrease in functional residual capacity in about 70% of patients post thoracotomy.¹⁰⁴

In cases of Lung resection, NIV use in the post-operative period significantly reduced need of re intubation and reduced mortality as demonstrated in a RCT by Auriant et al.¹⁰⁵ Stephan et al conducted a study in 830 post-cardiothoracic surgery patients with or at risk for respiratory failure.¹⁰⁶ Use of high flow nasal cannula (HFNC) therapy was compared with intermittent NIV. It did not result in worse rate of treatment failure defined as need for reintubation.¹⁰⁶ A meta-analysis of 14 trials by Zhu et al, included 1740 patients and showed

that NIV had no significant effect in the treatment of patients after cardiothoracic surgery. But NIV improved oxygenation and reduced chances of reintubation.¹⁰⁷

NIV in early oesophageal surgery is a relative contraindication for application of positive pressure at high level with risk of loss of integrity oesophageal sutures.^{108,109} A systematic review of literature conducted by Charlesworth et al could not find enough evidence for or against the use of NIV following oesophageal surgery.¹¹⁰

Recommendations

In cardiothoracic surgeries, use of NIV is recommended post operatively for acute respiratory failure to improve oxygenation and reduce chance of reintubation. (2A)

NIV should not be used in patients undergoing esophageal surgery. (UPP)

Role of NIV in post lung transplant

During post-operative period of lung transplant, graft and recipient-related respiratory difficulty requiring mechanical ventilation is a common scenario and can present within hours to days. Prolonged intubation in these immunocompromised patients is one of the main predisposing factors for developing nosocomial pneumonia, leading to prolonged ICU stay with significant morbidity and mortality. Non-invasive mechanical ventilation is recommended to shorten weaning time and to avoid reintubation following lung transplantation.¹¹¹⁻

Recommendations

NIV may be used for shortening weaning time and to avoid re-intubation following lung transplantation. (2B)

NIV during Procedures (ETI/Bronchoscopy/TEE/Endoscopy)

Patients with hypoxemic ARF may need to undergo various procedures for different indications. NIV decreases the rate of complications in patients undergoing bronchoscopy. In a small study (6 patients), Agarwal et al demonstrated that bronchoscopy can be safely performed in hypoxic patients with ARF.¹¹² Two other studies also came to the same conclusion.^{113,114} In a retrospective study of 27 patients who underwent bronchoscopy under NIV support, Sircar et al demonstrated that it is feasible to perform bronchoscopy in hypoxemic patients, thus avoiding ETI.¹¹⁵

In an RCT, Baillard et al studied the effect of NIV for preoxygenation prior to ETI. Patients had better arterial oxygenation prior to and after intubation when preoxygenated with NIV as compared to non re-breather bag mask.¹¹⁶ In another multicentre RCT, Jaber et al used preoxygenation by NIV as a part of intubation protocol.¹¹⁷ These patients had lesser complications. Similar results were seen in an RCT involving morbidly obese patients undergoing ETI.¹¹⁸

Recommendations

NIV may be used for pre-oxygenation before intubation. (2B)

NIV with appropriate interface may be used in patients of ARF during Bronchoscopy/Endoscopy to improve oxygenation. (3B)

NIV in Viral pneumonitis ARDS

The role of NIV in acute respiratory failure, caused by H1N1 influenza has remained controversial. Initial studies did not recommend the use of NIV in H1N1 pneumonia.^{119,120,121} However, subsequent clinical experience and studies found good success rate with the use of NIV.

A Spanish registry of 148 patients with H1N1 pneumonia, NIV was used in 177 patients (25.8%) with a success rate of 40.7%. Low APACHE, low SOFA scores, no vasopressor requirement, absence of renal failure, fewer than 2 chest X-ray quadrant opacities were associated with NIV success. NIV success was associated with shorter hospital and ICU stay, and lesser mortality.¹²² Rodriguez et al did secondary analysis from prospective and observational multicentre trials of 1898 patients with hypoxemic respiratory failure due to influenza and found that NIV failure was 56.8%. APACHE II score, SOFA score ≥ 5 was associated with failure.¹²³ Also, ICU mortality was higher in subjects with NIV failure, compared with invasive ventilation and NIV failure was associated with higher ICU mortality. A recent small cohort study of 43 patients of H1N1 pneumonia requiring NIV seconded the same findings and also found association of use of corticosteroids and early hemodynamic failure to be associated with NIV failure.¹²⁴ Also they concluded that NIV failure was associated with increased mortality.

Recommendations

NIV cannot be considered as a treatment of choice for patients with acute respiratory failure with H1N1 pneumonia. However, it may be reasonable to use NIV in selected patients with single organ involvement, in a strictly controlled environment with close monitoring. (2B)

NIV and Acute exacerbation of Pulmonary Tuberculosis

NIV has been used for long term and domiciliary ventilations in patients with sequelae of pulmonary tuberculosis, and also for acute exacerbation of TB sequelae.¹²⁵ However, its use in acute exacerbation of active pulmonary TB remains a controversial issue. Very few published reports and articles are available for the same. Agarwal et al reported 3 cases of successful treatment of tuberculous ARDS with NIV delivered with face mask.¹²⁶ However, the main concern with use of NIV in TB is the potential risk of transmission of TB. Another concern is the prolonged need of NIV and higher risk of pneumothorax and haemoptysis.

Recommendations

Careful use of NIV in patients with acute Tuberculosis may be considered, with effective infection control precautions to prevent air-borne transmission. (3B)

NIV after planned extubation in COPD patients

Characteristic feature of COPD is persistent reduction in expiratory flow which is not fully reversible. It causes 'air trapping' and progressive hyperinflation of the lungs and flattening of the diaphragm. This leads to change in dynamics of the breathing precipitating chronic respiratory failure. As the disease progresses, patients are prone to experience exacerbations and frequent respiratory failure especially hypercapnic failure. Due to frequent infections, catabolic state with malnutrition and muscle wasting;

COPD patients are difficult to wean from the invasive ventilation and have more chances to have extubation failure and reintubation. Nava et al. (2005) in their multicentre randomized controlled trial compared standard medical therapy versus immediate post-extubation NIV use in selected high-risk population for re-intubation. They found that, use of NIV in this population reduces the need for reintubation and significantly decrease in intensive care as well as in-hospital mortality.²¹⁵ Khilnani et al. (2011), conducted a randomized controlled trial to study the effect of NIV immediately post extubation in COPD patients.²¹⁶ They observed that there was less frequent need for reintubation in patients treated with NIV but ICU and in-hospital stay was same in both groups. In a multicentre randomized trial, C. Girault et al. (2011) investigated effectiveness of NIV as early weaning/ extubation technique in difficult to wean patients having chronic hypercapnic respiratory failure.²¹⁷ They assigned patients in 3 groups; conventional weaning on invasive ventilation, extubation followed by standard oxygen therapy and extubation to NIV. They found that weaning failure rate along with post-extubation acute respiratory failure rate were significantly less in the NIV group. In Cochrane systematic review, Burnset al. studied trials comparing extubation followed by immediate NIV to continued invasive weaning on mechanical ventilation.²¹⁸ They included 16 studies with 994 patients and interpreted that weaning to NIV reduces rate of death and pneumonia without increasing risk of weaning failure and reintubation. Mortality benefits were significantly greater in COPD patients in comparison to other subgroup population.²¹⁸

High Risk Patients²¹⁵

- More than one consecutive failure of weaning trial
- Chronic heart failure
- PaCO₂ >45 mm Hg after extubation
- More than one co-morbidity (excluding chronic heart failure).
- Weak cough defined as Airway Care Score values ≥8 and <12
- Upper airways stridor at extubation not requiring immediate reintubation.

Recommendation

We recommend that NIV may be used to wean high risk patients from invasive mechanical ventilation as it reduces re-intubation rate. (2B)

NIV for respiratory distress post extubation:

Post extubation respiratory failure is one of the dreaded complications requiring reintubation, more chances of developing

pneumonia, prolonged ICU stay and even have high mortality rate. There are many underlying reasons for the development of respiratory failure post extubation, of which unresolved primary condition, multiple comorbidities, development of pneumonia, and dependency on mechanical ventilation are a few common causes.

Esteban et al. conducted multicentre randomized controlled trial to evaluate the role of NIV in respiratory failure post extubation. The trial was stopped early after the interim analysis showed no difference in the rate of reintubation but there was increased intensive care mortality in NIV group as compared to standard medical treatment.²¹⁹

Keenan et al (2002) conducted a randomized controlled trial to determine the role of NIV in preventing the need for reintubation in high risk patients developing respiratory failure post 48 hours of extubation. There was no difference in the rate of reintubation or hospital mortality in both groups.²²⁰

Meta-analysis done by Changyang Lin et al (2014) studied 10 trials involving 1382 patients. They observed that NIV in established respiratory failure post extubation did not decrease the reintubation rate and ICU mortality compared to standard medical therapy.²²¹

Recommendations

We recommend that NIV therapy should not be used to manage respiratory distress post-extubation in high risk patients. (2B)

CONTRAINDICATIONS OF NIV

Most contraindications have been determined by the fact that they were the exclusion criteria in many studies.^{127,128} (See Table 3)

PREDICTORS OF NIV FAILURE

Although use of NIV is safe, it needs careful observation to detect failure at the earliest. Various studies have evaluated the risk factors/predictors of NIV failure.

Various studies have shown the following criteria for NIV failure:^{129,130}

- High severity score of illness (APACHE II, SAPS II, SOFA scores)
- Older age
- Failure to improve after 1 hour on NIV
- Multiorgan involvement
- Premorbid status (inability to perform self care)
- Mean pH < 7.25, mean PaCO₂ ≥ 75 mmHg after 2 hours of NIV initiation, in patients with hypercapnic failure.
- Difficult to identify the etiology of acute respiratory failure

Table 3: Clinical scenarios of Contraindications for the use of NIV

Sr. No.	Contraindications	Examples
1.	Inability to protect the airways	Comatose patients, Cerebrovascular Accident (CVA) with bulbar involvement, Confused and Agitated patients.
2.	Hemodynamic instability	Uncontrolled Arrhythmia, Patient on very high doses of Inotropes or Vasopressors with presence of shock.
3.	Inability to fix the interface	Facial abnormalities, Facial burns, Facial trauma, Facial anomaly.
4.	Severe GI Symptoms	Severe Vomiting, Obstructed bowel, Severe Hematemesis.
5.	Massive Hemoptysis	
6.	Copious secretions	
7.	Post-cardiac Arrest	

- ARDS / pneumonia as the etiology
- PaO₂/ FiO₂ < 150 mmHg
- Higher Tidal volume generation.

In patients with early ARDS, SAPS II >34 and the inability to improve PaO₂/FiO₂ after 1 hr of NPPV were predictors of failure.¹³¹ In a secondary analysis of a multicentre observational study of NIV in 806 patients of confirmed Influenza Infection, found high APACHE II and a SOFA score \geq 5 as a risk factor for NIV failure.¹³²

Similarly, The Efrain multinational prospective cohort study of immunocompromised patients with acute hypoxemic respiratory failure, showed that it is difficult to identify the aetiology of respiratory failure as an important predictor of NIV failure.⁸⁴

A prospective observational study of 62 patients, of de novo acute hypoxemic respiratory failure, showed that an expired tidal volume of more than 9.5 ml /kg of PBW, accurately predicts NIV failure.¹³³

In the post hoc analysis of RCT REVA study, Frat et al concluded that a PaO₂/FiO₂ below 200 and a high tidal volume > 9 ml/kg are strong predictors of NIV failure in patients with acute hypoxemic respiratory failure.¹³⁴ Multivariate analyses of the recent multicentre randomised ENIVA trial concluded that high minute ventilation was a risk factor for NIV failure.⁷⁹

Around 2015, a single centre cohort study, concluded that NIV failure was associated with increased ICU and hospital stay and an increased risk of in-hospital mortality.¹³⁵ Rodriguez et al analysed the use of NIV in confirmed influenza infection and found that ICU mortality increased in patients with NIV failure.¹³²

Recommendation

NIV failure is an independent risk factor for mortality, thus we recommend careful patient selection for initiating non-invasive ventilation. (UPP)

APPLICATION OF NIV

Modes of NIV

General Considerations

With the advancement of NIV, more and more modalities are now available for ventilating the patients. Same modalities with different names exist in different machines, thus complicating the situation further.

NIV devices have 2 types of triggers- “flow based” and “pressure based”. Minute ventilation, respiratory pattern, dynamic lung compliance and resistance and changes in end-expiratory lung volume were the same with the two triggering systems.¹³⁶ Flow triggering has shorter trigger delays and better synchrony.^{136,137}

In COPD, flow triggering has been found to reduce the autoPEEP and inspiratory effort during both PSV and A/C modes compared with pressure triggering.¹³⁶

Recommendation

We suggest using flow trigger over pressure triggering in assisted modes, as it provides better patient ventilator synchrony. Especially in COPD patients, flow triggering has been found to benefit auto PEEP. (3B)

Ventilation delivered by Non Invasive ventilators is either volume targeted or pressure targeted. There is no specific difference in the efficacy of either modalities.

Volume targeted ventilation provides more assured tidal volumes, despite changing lung mechanics. However, these modes fail to compensate the air flow for patient’s varying needs, and circuit leaks. They are not used routinely by most care givers. Pressure targeted ventilation assures better delivery of tidal volume in systems with leaks and helps improve patient comfort and synchrony, with patient controlled inspiratory flows.¹³⁸ Recent availability of hybrid variety of modality ‘Volume-targeted pressure ventilation’, helps to combine the advantages of both.¹³⁹ Both modalities of delivery have been equally efficacious in decrement of CO₂ levels, with no difference in the intubation rates and hospital mortality in a chinese prospective randomised controlled trial of acute hypercapnic failure.¹⁴⁰

Recommendations

Pressure-targeted modes are preferred over volume-targeted to deliver ventilation in presence of air leaks, as they help to maintain TV better. (3B)

In patients who need high pressures for chest inflation (restrictive disease, severe chest deformity, obese), volume-controlled ventilation mode is more effective. (UPP)

Non-invasive ventilatory breaths may be either timed cycled, or flow-cycled. Presence of a large leak in the NIV, interferes with the flow cycling of the ventilator. Time cycled breaths have shown to provide better synchrony in presence of large leaks, as shown in lung model studies and small clinical studies.^{138,141}

Recommendation

When large leaks are present, we recommend to switch over to pressure targetted modes with time cycling, to provide better synchrony (3B).

Newer Modes

Newer modes of NIV mainly are Average volume assured pressure support (AVAPS), Intelligent volume assured pressure support ventilation (iVAPS), Proportional assisted ventilation (PAV), Adaptive servo ventilation (ASV), And use of Neurally-adjusted ventilatory assist (NAVA).

Average Volume Targeted Pressure Support (AVAPS)

As compared to BPAP, BPAP with AVAPS have been shown to help rapid recovery of consciousness in patients with COPD and hypercapnic encephalopathy.¹⁴² However, a recent multicenter RCT failed to demonstrate any significant difference in CO₂ levels, intubation or in-hospital mortality with the use of AVAPS as compared to PS mode in patients with acute hypercapnic respiratory failure.¹⁴⁰ Another pilot study to evaluate the feasibility of AVAPS in patients with COPD and acute hypercapnic failure, concluded that AVAPS may be used in this group of patients, but predictors of failure included higher baseline APACHE II scores and non-significant improvement in PaCO₂ in the first 2 hours of treatment.¹⁴³ Another small Turkish study, of patients with acute hypercapnic respiratory failure, included 33 and 29 patients in AVAPS-S and BPAP-S group, found more reduction in PaCO₂ levels in the AVAPS-S group, however, the course was same in both the groups.¹⁴⁴ Similarly, in 50 super obese patients, there was no difference between AVAPS and NIV PS mode, in terms of daytime PaCO₂ at 3 months, and day time quality of life and fat

mass reduction.¹⁴⁵ Selim et al reviewed 120 relevant articles and concluded that AVAPS when compared to ASV, was found to deliver more consistent minute ventilation and can be recommended for sleep related hypoventilation disorder.¹⁴⁶

Recommendations

AVAPS may be tried in patients in selected acute hypercapnic failure patients, under close supervision (3B)

Proportional assist ventilation (PAV)

Proportional assist ventilation (PAV) is a newer mode that delivers assisted ventilation in proportion to patient effort. Studies have failed to prove any benefit in reducing intubation rates, hospital stay or mortality, however, they do report better patient comfort and patient-ventilator synchrony with the use of PAV with NIV, as compared to PS mode.^{147,148} A recent systemic review and meta-analysis of 14 RCTs with 931 subjects, failed to reveal enough evidence for use of NIV-PAV in critically ill adults.¹⁴⁹

Recommendation

There is not enough evidence to support the use of NIV-PAV in acute setting over PS mode. (1A)

Adaptive Servo Ventilation (ASV)

Selim Bet al. reviewed 120 relevant articles and concluded that ASV may be used to treat central sleep apnoea syndromes as it provides a more steady breathing airflow pattern.¹⁴⁶ A recent randomised trial, with 74 patients with AECOPD, found using NIV with ASV was equally successful as PSV.¹⁵⁰

Recommendation

There is not enough evidence to support the use of NIV-ASV over PSV. (1A)

Neurally adjusted ventilatory assist (NAVA)

Neurally adjusted ventilatory assist (NAVA) is a novel ventilatory mode that utilizes the electrical activity of the diaphragm to pick up respiratory signals and deliver assistance in proportion to the patient's ventilatory requirement.¹⁵¹ In a systemic review of studies (9 studies – 96 subjects), comparing the use of PSV versus NAVA during NIV for acute respiratory failure, revealed a significantly higher asynchrony index and a 3.4 % times higher risk of severe asynchrony with PSV.¹⁵² Similar findings were found in a randomised study of 40 subjects with AECOPD, showing better patient-ventilator synchrony with use of NIV-NAVA as compared to NIV-PS.¹⁵³ However, there was no difference in the gas exchange, duration of NIV, length of hospital stay and rate of NIV failure.

Recommendation

Non-invasive NAVA with mask / helmet, may be used to improve patient ventilator synchrony in patients with acute respiratory failure, depending on its availability and operator familiarity (UPP).

MANAGEMENT OF PATIENT ON NIV

Sedation

A Cochrane review of 2014 on the role of NIV as a weaning strategy from invasive mechanical ventilation found only one study that used a standardised sedation protocol before or after initiation of NIV.¹⁵⁴ Matsumoto et al retrospectively evaluated the role of sedation in agitated patients treated with NIV after an episode of acute respiratory failure.¹⁵⁵ Of 3506 patients who received NIV, only 3.4% (81 patients with non-intubation code [DNI] and 39 non-DNI) were sedated either intermittently or by continuous infusion. Drugs used were Risperidone or haloperidol for intermittent use and dexmedetomidine, midazolam or propofol for continuous infusion, titrated as per RASS scores. The authors concluded that sedation is potentially useful to avoid NIV failure in both groups of patients (DNI and non- DNI).¹⁵⁵ An international prospective, observational multicentre study involving 322 ICUs in 30 countries, found that analgesia and sedation, either individually or combined, were used only in 19.6% of patients during NIV. They found when used alone, sedatives and analgesics are safe. However, their simultaneous use was found to be associated with NIV failure.¹⁵⁶

In post extubation patients, use of sedation and/ or analgesia to improve interface tolerance, was found to decrease the rate of NIV failure, hospital mortality and ICU LOS.¹⁵⁷

Drugs which have been used in trials are dexmedetomidine, Propofol, Remifentanyl, and have been found safe and effective to use.^{158,159,160}

Recommendations

A non-pharmacological approach to calm the patient (Reassuring the patient, proper environment) should always be tried before administering sedatives. (UPP)

In patients on NIV, sedation may be used with extremely close monitoring and only in an ICU setting with lookout for signs of NIV failure. (UPP)

Sedation in patients on NIV if used appropriately and with the correct precautions improves patient comfort and reduces chances of NIV failure. (3B)

No preference of any drug can be recommended specifically for use in patients with ARF on NIV. (3B)

Discharge

The discharge process for patients requiring long term non-invasive ventilation requires meticulous planning and execution to prevent re-admissions to the health care. The protocol should be individualised for every patient, with adequate training and education of the care givers. Also round the clock health care service should be available.

Recommendation

For patients needing long term home NIV, an individualized plan with a plan matrix should be organized, involving all concerned parties, with clearly defined roles. Education and training of the care giver, round the clock technical support, are the minimum pre-requisites before planning to discharge the patient on NIV. (UPP)

Transport

Recent reports from the Australian Helicopter Medical services, involving 3018 missions, in which there were 106 cases of NIV therapy during the retrieval revealed that none of these patients died or were intubated en route.¹⁶¹ These results demonstrate the growing safety of NIV in interhospital transport using NIV in patients with ARF, key however being proper patient selection.

Recommendations

Inter-hospital and Intra-hospital transport of patients on NIV may be considered only if absolutely necessary. (3B)

Infection transmission with NIV

Experimental model studies have shown that the dispersion distance of exhaled air particles from patients on NIV via the ResMed Ultra Mirage Mask was 0.5mm, along the exhalation port.¹⁶² Another human-patient simulator (HPS) study, showed the maximum dispersion distance of approximately 0.95 m with different face masks, with a more diffuse dispersion with use of whisper swivel exhalation port.¹⁶³

A clinical study evaluated the characteristics of droplet/aerosol dispersion in 3 groups of subjects and concluded that NIV and chest physiotherapy are droplet (not aerosol generating procedures, producing droplets > 10µm in size, which fall out within 1 metre. Oxygen therapy did not increase the droplet count in any size range. Whereas, a nebuliser produces aerosols of small and medium size.¹⁶⁴ Similarly, a retrospective case control study by Yu and colleagues, concluded that use of NIV was not a significant contributory factor for spreading of infectious agents during the SARS epidemic in China.¹⁶⁵

When use of helmet and face mask as an interface were compared, on a human patient simulator model with mild lung injury, the use of helmet with good seal around the neck was found to have limited exhaled air leak and dispersion.¹⁶⁶ While using nasal masks, air leakage also occurs through the mouth, besides the exhalation valve.¹⁶⁷ Choosing the correct size of the interface, with the best fit helps minimise the unintended air leaks. Higher ventilator pressures increase the range of dispersion of exhaled air and amount of air leakage around the interface.¹⁶³ Other measures which have been useful in reducing the risk of nosocomial transmission of infection with use of NIV include using a dual limb circuit. The bias flow in the single limb circuits, prevents re-breathing and increases circuit leaks, thus also increasing dispersion of infected particles in the air.¹⁶² Adding a viral-bacterial filter between the mask and exhalation port has also been found useful to prevent infectious transmission. However, the risk of frequent blockage of the filter with moist secretions makes its use difficult.¹⁶⁸ However, pulmonary TB infective particles are 1- 5 µm in diameter and spread throughout the room by air currents. Due to relatively long period of infectivity of TB, until the diagnosis and at least 2 weeks after initiation of anti-TB treatment, such patients need to be isolated in negative pressure isolation rooms with HEPA filters and ultraviolet germicidal irradiation (UVGI).¹⁶⁹

Recommendations

Apart from personal protective equipment (N95 mask, gown, gloves, eye protection) and hand hygiene, we recommend the

following precautions to be taken when using NIV on a patient with infectious disease: (3 B)

- Minimise leaks in the circuit.
- Non-vented face mask, or a helmet – with the best fit to the facial contour.
- Secure the mask, prior to turning on the ventilator. Turn off the ventilator before removing the mask.
- A viral/bacterial filter (to filter particles 0.3 mm in size) at the outlet of the ventilator and also at the expiratory side of the circuit.
- Complete decontamination of the ventilator before use in other patients.

EQUIPMENT FOR NIV AND MAINTENANCE OF NIV EQUIPMENT

Ventilators

Use of non-invasive ventilators peaked during the polio epidemic of the 1950s, when negative pressure non-invasive ventilation helped to improve survival.¹⁷⁰ It was only after early 2000s that the positive pressure non-invasive ventilators became popular in the acute care setting.¹⁷¹ Any ventilator, designed to compensate for air leaks, can be used for delivering non-invasive ventilation. Most old invasive critical care ventilators, failed to compensate for the leaks and hence were not suitable for delivering non-invasive ventilation.¹⁷² In current critical care non-invasive ventilators with leak compensation, dual limb circuits with segregation of inspiratory and expiratory gases are used. In bi-level ventilators, a single limb circuit, with a leak port which serves as a port for passive exhalation is used. "Intermediate" ventilators have more recently been developed, which have combined features of bi-level, home and ICU ventilators, with wider range of inspiratory and expiratory parameters and volume as well pressure targeted ventilation.¹⁷³ A comparison of different ventilators used for delivering NIV is shown in Table 4.

Initial clinical studies, found no differences in the work of breathing, respiratory rate, minute ventilation or PaCO₂ between a bi-level ventilator and a critical care ventilator, when similar pressure settings were used.^{174,175}

Recommendations

We recommend that bilevel ventilators or specifically designed ICU ventilators with non-invasive mode should be used for delivering Non-invasive ventilation in critically ill patients. (UPP)

Both critical care ventilators with leak compensation and bi-level ventilators have been equally effective in decreasing the WOB, RR, and PaCO₂. (3B)

The CO₂ rebreathing is a major concern when using bilevel ventilators with a single limb for delivering non-invasive ventilation. Following methods may help reduce the CO₂ rebreathing which include:

- Leak port for exhalation in the mask than in the circuit/hose.¹⁷⁶
- Titration of the oxygen in the mask than at the ventilator end. Though this affects the FiO₂ delivery negatively.¹⁷⁷
- Higher expiratory pressure.¹⁷⁸
- Use of an exhalation valve (but also increases expiratory resistance).¹⁷⁹

Table 4: Comparison between different ventilators used for the purpose of Non-Invasive Ventilation

	<i>Bilevel ventilators</i>	<i>Critical Care Ventilators</i>	<i>Intermediate non-invasive ventilators</i>
Gas Source	Compressor / Electronic turbine pump	High pressure Gas Source	Compressor / Electronic turbine pump
Circuit	Single limb	Dual limb	Single/ Dual Limb
Exhalation valve	Passive exhalation valve (Whisper Swivel)	Active exhalation valve	Active exhalation valve
Type of ventilation	Old models provided only pressure targeted ventilation. Newer models provide volume targeted ventilation as well.	Volume and pressure targeted ventilation	Volume and pressure targeted ventilation
Advantages	<ul style="list-style-type: none"> • Portable. • Easy to use. • Most Home Ventilators 	Predictable FiO ₂ delivery	Predictable FiO ₂ delivery
Disadvantages	<ul style="list-style-type: none"> • Unpredictable FiO₂ delivery, as lacks a blender. May fail in patients with high O₂ requirement. • Risk of rebreathing, due to single limb. 	<ul style="list-style-type: none"> • Lack of leak compensation, affects the smooth functioning. • Newer ICU ventilators have "NIV modes" with leak compensation 	Some have an incomplete dual limb circuit, in which the expiratory limb is only a short tube with a PEEP valve. This has negative effects on triggering and cycling.

Recommendations

It is advisable to have leak port in the mask rather than the hose in order to reduce re-breathing in single limb bi-level ventilators. (3A)

The expiratory pressure should be kept minimum 4cms H₂O to prevent re-breathing. (3A)

Interface

The NIV interfaces currently available are nasal mask/pillows, oronasal mask, total-face mask, mouthpiece, and helmet. Bench studies and computerised calculations have shown a massive difference in the internal volume and the effective dead space of the mask.^{180,181} However, clinical and physiological studies found no difference in terms of the effect of this dynamic dead space on the patient effort, arterial blood gases, gas exchange and minute ventilation.¹⁸² Helmet when used as an interface has shown to interfere with triggering and cycling off delays, this leading to patient ventilator dyssynchrony.¹⁸³ But using higher pressures in the helmet abolished these delays.¹⁸⁴ Also, a meta-analysis in 2016, did not show an increase in the PaCO₂ levels in patients with hypercapnic respiratory failure.¹⁸⁵

Recommendations

Interfaces used for NIV may be interchangeable in clinical practice provided; adjustments of the ventilatory device parameters are performed. (3B)

In an acute setting, the choice of interface is based on the patient tolerance, staff experience and the fit on the face based on facial features. However, nasal masks/ pillows and mouthpiece, are not preferred due to predominance of mouth breathing. Web based survey in Europe and North America, showed that oro-nasal mask was most commonly used, up to 70%.¹⁸⁶ Another study in Brazil, reported the predominant use of oronasal and total face masks.¹⁸⁷

The recent use of helmet has shown to offer advantages like less down time, and better airway clearance and also allows patients to drink and communicate. A systemic review and meta-analysis of 11 randomised and case control studies, comprising 621 subjects

showed lower intubation rates, lower hospital mortality and less complications with the use of helmet.¹⁸⁵ This reduction in intubation rates was seen in both hypercapnic and hypoxemic patients, independent of the ventilatory mode used. Another meta-analysis showed similar benefits in terms of intubation rates and hospital mortality, in patients with hypoxemic non-hypercapnic acute respiratory failure.¹⁸⁸ A recent RCT by Patel et al, of subjects with ARDS, use of helmet reduced intubation rates, improved ventilator free days and improved mortality, over the use of face mask, without increase in the interface associated complications.¹⁸⁹ Thus helmet appears promising in patients requiring higher pressures, however, further training of the medical team is necessary before its use.

Recommendations

Currently, Oronasal mask is the most preferred interface for non-invasive ventilation for acute respiratory failure. (2A)

A major challenge for patient co-operation for use of NIV is improving the patient comfort and reducing the risk of skin breakdown and damage. Beginning of skin breakdown has been seen within only 24 hours of use of NIV.¹⁹⁰ A simple and effective strategy to prevent skin damage is to leave enough space to allow 2 fingers to pass between the skin and interface.¹⁹¹ A small amount of air leak should be acceptable for the same. A study by Weng of 90 participants, showed the equal efficacy of hydrocolloid and polyurethane dressings in preventing facial pressure ulcers during use of NIV.¹⁹² In a small Chinese RCT of 60 patients, similar findings were confirmed.¹⁹³ Bishopp et al showed significant reduction in the risk of developing grade 2 pressure ulceration, with the early, prophylactic use of hydrocolloid nasal dressing.¹⁹⁴ The study was a quality improvement project and the findings were compared retrospectively to previous 12 months admission. A recent RCT of 152 patients, showed maximum efficacy with the application of hyper oxygenated fatty acids (HOFA) in prevention of NIV related pressure ulcers, as compared to adhesive thin and foam dressing.¹⁹⁵ A recent meta-analysis of RCTs, consisting of 1260 patients, found use of hydrocolloid dressing to significantly decrease the incidence of facial pressure ulcers.¹⁹⁶

Recommendations

All interfaces used should be made of soft material. Cushioning of skin in contact with the interface may be done with hydrocolloids, foam pad, or transparent dressing. (3A)

All patients on NIV should undergo periodic skin assessment of pressure points, every 4-6 hourly. (UPP)

Humidification

Heat Moisture exchanger (HME) and heated humidifiers (HH) are used for providing humidification in patients on NIV. Use of HME has found to produce higher absolute humidity levels of the upper airway.¹⁹⁷ However, use of HME has found to increase the WOB, rebreathing and PaCO₂ levels.¹⁹⁸ A survey of 15 hospitals, revealed that HHs are used more often with NIV.¹⁹⁹ However, a recent multicentre RCT of 15 centres, 247 patients – found no significant difference between the use of HME and HH in regards to mucosal dryness, intubation rate, PaCO₂, NIV duration, ICU and hospital LOS, or ICU mortality.²⁰⁰ This study though was underpowered. The risk associated with the use of HME, is its frequent blockage with moist secretions, and the added resistance to breathing.

Recommendation

Humidification is routinely not required in patients on NIV. However, patients who complain of dryness of respiratory tract, or thick tenacious secretions, heated humidification or HME may be considered. (3B)

Aerosol Delivery

Use of aerosol is an integral part of therapy in COPD, asthma. Aerosol delivery is affected by leaks, inspiratory flow rates and position of expiratory port. Data is lacking to comment if use of nebulisers or MDI is better for aerosol delivery with NIV. The most favourable position for placement of the nebuliser for an optimal deposit is to put the nebulisation device between the interface and the respiratory circuit.^{201,202}

Recommendation

We advise placing the nebuliser between the mask with/without expiratory port and the respiratory circuit. (3A)

Cleaning and Disinfection of Accessories

Cleaning, rinsing and drying of the equipment of NIV, is important to prevent cross-infection. Disposable parts should not be re-used.

Recommendations

We advise cleaning and disinfection of non-invasive ventilators and its accessories should be as per manufacturer's recommendations. The standard of care should be followed, and proper documentation maintained. (UPP)

PRACTICAL APPLICATION

Initiation and Customisation

Assess the need of NIV

Before application of Non-invasive ventilation, it is important to assess the need of NIV. In addition to the rest of the medical

Table 5: 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

treatment, NIV should be applied simultaneously to a patient in acute respiratory failure (ARF), based on the clinical criteria (Table 5), provided there is no contraindication. NIV should only be considered if there is enough evidence of its effectiveness in that particular disease condition.

NIV is initiated mostly in the emergency department, intensive care unit and HDU. NIV has been found to be most effective in COPD. NIV should be initiated in COPD when pH < 7.35 and pCO₂ > 45 mmHg persists or develop despite optimal medical therapy. Severe acidosis is not a contraindication to NIV so long as the expertise to perform safe endotracheal intubation is readily available. The lower the pH the more chances of failure. One should not delay intubation when it is indicated.

Current guidelines recommend CPAP or bilevel NIV for patients with ARF due to cardiogenic pulmonary edema. There is uncertainty of evidence to recommend the use of NIV for ARF due to asthma. NIV can be used for patients with post-operative ARF. NIV is recommended for dyspnoeic patients for palliation in the setting of advanced cancer or other terminal conditions. NIV has been applied for chest trauma patients with ARF with success. NIV is recommended to prevent post-extubation respiratory failure in high-risk patients. NIV should not be used in the treatment of patients with established post-extubation respiratory failure.

Recommendations

NIV therapy should be initiated for patients in Critically Monitored Area like ICU, HDU, ER, and Respiratory Wards with adequately trained staff. (UPP)

Arterial blood gas (ABG)

ABG is usually used to judge the effectiveness of NIV especially in cases of Acute Hypercapneic Failure. ABG monitoring should be done within one hour after initiation of NIV therapy. Repeat Frequency should be based on the clinical condition of the patient, first ABG findings and NIV settings.

Recommendations

We recommend first ABG within first hour of NIV therapy. After this, the frequency should be based on clinical condition of patient. (UPP)

Level of consciousness

A severely altered level of consciousness especially in hypoxemic respiratory failure is considered to be a possible contraindication to non-invasive ventilation. To assess level of consciousness with the use of Glasgow Coma Scale (GCS), ability to cough out secretions and maintain airways are important to assess before and after application of NIV.

Mariko et al. in 2018 conducted a study on 237 patients on NIV, they divided the patients in two groups, one with normal level of consciousness (NLC) with GCS 15 and Altered level of

consciousness (ALC) with GCS 14 or less, patients with GCS less or equal to 8 were excluded considering safety reasons and need for intubation, they also used Kelly-Matthay scale.²⁰³ Eighty-nine patients were excluded because of underlying respiratory disease (n=74) and the need for urgent intubation (n=15). Among the 148 included patients, 66 had ALC and 82 did not. They concluded that with careful monitoring and management NIV may be successfully applied in patients with mild ALC during episodes of hypoxemic respiratory failure.

Scala et al in 2005 did a case control study on eighty of 153 consecutive COPD patients requiring NIV for ARF which were divided into four groups depending on Kelly-Matthay scale.²⁰⁴ They confirmed that NIV may be successfully applied in patients with COPD exacerbations with milder ALCs, whereas the rate of failure in patients with severely ALCs (i.e., Kelly score > 3) is higher; even though better than expected, so that an initial and cautious attempt with NIV may be performed even in this latter group.

The Kelly-Matthay scale ranges from Grades 1 to 6 with Grade 1- alert, follows complex 3-step commands; Grade 2- alert, follows simple commands; Grade 3- lethargic, but arousable and follows simple commands; Grade 4- stuporous, only intermittently follows simple commands even with vigorous attempts at arousal; Grade 5, comatose, brain stem intact; grade 6, comatose with brainstem dysfunction.^{204,205}

Recommendation:

We recommend that the consciousness level of the patient should be assessed with GCS. (2A)

Delirium

Charlesworth et al performed a systematic review and meta-analysis of the literature to determine the prevalence of delirium in patients on NIV and its impact on patients on NIV. They conclude that data related to this is scarce and of low quality. Though the data was of low quality, there was high reported prevalence of delirium and the association with NIV failure lends support for more awareness and more routine screening.²⁰⁶ Multinational survey conducted by Tanaka et al. in 2015 also strongly reemphasize poor efforts towards delirium assessment and management in the intensive care unit setting, especially regarding patients on NIV.²⁰⁷

Recommendations

We recommend delirium monitoring should be done with CAM-ICU score for NIV success. (UPP)

Transcutaneous CO₂

Transcutaneous CO₂ is a continuous pain-free monitoring of CO₂ measurements and may replace the frequent need of ABGs for CO₂ measurement that is more painful, requires frequent puncture leading to technical expertise, bleeding, hematoma and is snapshot measurement

Retrospective analysis of Patients on NIV in Emergency Department done by Horvah et al., published in Swiss Medical Weekly on 26th October 2016, concluded that transcutaneous PCO₂ monitoring shows a good concordance with PaCO₂ and is a reliable, feasible, patient-friendly and safe alternative to repeated blood gas analysis for patients with severe hypoxaemic and/or hypercapnic respiratory failure receiving emergency NIV in the ED.

Table 6: Clinical criteria to be met by patients before Weaning is attempted.

S. No	Measure	Character
1.	Arterial pH	≥ 7.35
2.	SpO ₂	> 90%
3.	Respiratory Rate	≤ 25 / min
4.	Heart rate	≤ 120 / min
5.	Systolic blood pressure	≥ 90 mmHg
6.	Signs of respiratory distress	No agitation, diaphoresis, anxiety

In addition, it can be used to adapt NIV settings in real time. An initial ABG to evaluate the respiratory and metabolic state and to rule out a significant discrepancy compared with the transcutaneous measurement is recommended.²⁰⁸

One Pilot observational study concluded that continuous PtcCO₂ monitoring provides a promising alternative to repeated blood sampling in subjects requiring NIV for acute hypercapnic respiratory failure.²⁰⁹

Recommendations

Transcutaneous CO₂ may be used for monitoring patients of COPD in place of repeated ABG monitoring. (2B)

WEANING

NIV reduces respiratory muscle fatigue and improves ventilation. Its usage has increased during acute settings. Sometimes, patients having COPD, OSA, various neuromuscular disorders including critical illness myoneuropathy require NIV for prolong period. Weaning from NIV in these patients is a difficult and tedious job. Weaning needs to be started only when primary condition is better, and patient meets the clinical criteria shown in Table 6.^{210,211}

Protocol Based Weaning

Protocol based weaning strategies have been found to be more successful with shorter duration of NIV requirement and shorter ICU length of stay.

Jun Duan et al in their prospective randomized control trial compared protocolized vs physician directed weaning from NIV.²¹² They formulated the protocol and randomized the patients in two groups. Respiratory technicians in Protocol- derived weaning group initiated the weaning attempt as per the protocol and in other group weaning was done as per the physicians' decision. They observed that protocol directed weaning significantly reduced the duration of NIV as well as length of stay in the ICU.

Recommendations

We recommend that weaning from NIV may be done by a standardized protocol driven approach of the unit. (2B)

Weaning strategies

Varied Strategies for weaning from NIV has been described:

- Stepwise reduction in NIV duration.
- Stepwise reduction in NIV pressure support.
- Immediate withdrawal of NIV after stabilization.

Strategy

Stepwise reduction in NIV duration

This method involves progressively reducing the duration of NIV over a period of 3-4 days once the patient satisfies the criteria for weaning. Initially weaning should be carried during daytime with overnight ventilation. The daytime weaning can be divided into periods of 3 hours each and can be performed as follows – during first 24hrs in each 3 hours, one hour without NIV (except during night period), in the second day in each 3 hours, two hours without NIV (except during night period) and in the third day NIV can be used only during the night period. NIV may be discontinued on day 4 unless continuation is clinically indicated for example, few hours in daytime and six hours or more overnight.²¹³

Plant et al used this strategy of stepwise reduction in NIV duration: On Day One, used as much of NIV, Day Two, NIV was used for 16 hours (including 6-8 hours of overnight NIV), On Day three, 12hrs of NIV (including 6-8 hours of overnight NIV) and discontinued on Day 4.

Recently published study by Venkatnarayan et al weaning from NIV used 16 hours of NIV (Including 6-8 hours of Overnight) on Day of randomization, Day 2: 12 Hours of NIV (Including 6-8 hours of Overnight) and Day 3: Only overnight NIV was used and complete withdrawal on Day 4.²¹⁴

Stepwise reduction in NIV pressure support

This strategy involves gradual reduction (2-3cms of H₂O) of IPAP and EPAP over a period of 6-8hrs and removing NIV once the patient tolerates IPAP of 6-8cms of H₂O and EPAP of 4-5cms of H₂O. There are no studies comparing the effectiveness of stepwise reduction of duration versus stepwise reduction of pressure support, but both the strategies can be used in conjunction with each other.^{211,214}

Immediate withdrawal of NIV

This strategy involves immediate cessation of NIV once the patient stabilizes. Though it has potential advantage of shortening the duration of weaning process, the rates of failure of weaning and reinstatement of NIV can be higher. A randomized control trial by Lun et al compared immediate withdrawal of NIV to stepwise reduction and found success rate of weaning to be 56% and 74% respectively, although the data is statistically not significant.²¹⁰ Immediate withdrawal of NIV can be tried in patients who required NIV for a shorter duration of time and who have clinically recovered well.

Venkatnarayan et al in 2019 compared above three strategies for weaning from NIV in patients with COPD with acute exacerbation and hypercapnic respiratory failure.²¹⁴ They found that there was increased chance of weaning failure in immediate withdrawal group but without any statistically significant difference. Total duration of NIV use and length of stay was significantly less in group of immediate withdrawal and gradual reduction in pressure support group than stepwise reduction in NIV duration group.

Recommendations

We recommend that any of three weaning strategies may be adopted for weaning NIV in COPD patients. (2B)

CONCLUSIONS

Non-invasive ventilation has been recognised a very important modality in the management of acute respiratory failure. NIV should only be used if there is good quality evidence of its effectiveness in that particular condition and there is no contraindication. NIV can

be used for patients with ARF due to COPD cardiogenic pulmonary, post-operative ARF, palliation in the setting of advanced cancer or other terminal conditions, chest trauma with ARF and to prevent post-extubation respiratory failure in high-risk patients. NIV should not be used in the treatment of patients with established post-extubation respiratory failure. It is important to fine-tune the patient, interface, and ventilator. NIV can be delivered via portable pressure ventilator or the standard ICU type of ventilator found in most intensive care units (ICUs). Pressure modes are preferred because there are many advantages of pressure targeted modes like pressure delivered is constant and pressure targeted ventilation compensates for air leak. Monitor continuously the patient on NIV for the worsening sensorium, respiratory distress, tachypnea, and deteriorating blood gases, and intervene early because delay in intubation worsens outcome. Most complications are minor that can be managed easily, and so every attempt should be made to continue NIV. Weaning can be done by various methods with equal efficacy. Protocol based weaning strategies have been found to be more successful with shorter duration of NIV requirement and shorter ICU length of stay.

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