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Non-Invasive Respiratory Support Strategy in Adult with Acute Respiratory Failure

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Abstract

Patients with acute respiratory failure sometimes will need invasive mechanical ventilation (IMV). High demand events such as a pandemic will render the already limited bed in ICU unavailable for another patient who also needs IMV. Acute respiratory failure can be divided into hypoxemic respiratory failure and hypercapnic respiratory failure. Non-invasive strategies presently available for treatment of acute respiratory failure are non-invasive ventilation (NIV), continuous positive airway pressure (CPAP) and High flow nasal oxygen (HFNO). Strong evidence has been present for the use of NIV in acute exacerbation of COPD, cardiogenic pulmonary edema and ARF in immunocompromised while in hypoxemic respiratory failure, low-moderate certainty of evidence pointing at the benefit of CPAP and HFNO. Using correctly and selectively the use of these non-invasive strategies can reduce mortality and prevent intubation.

Keywords: ARF, NIV, CPAP, HFNO

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INTRODUCTION

Covid-19 pandemic has exposed a huge gap in our capacity of treating acute respiratory failure (ARF). During the pandemic even developed countries struggled to provide intensive care and respiratory support due to high demand. Eventually, this condition also depleted resources for non-Covid respiratory failure patients. Such a situation necessitated tiered respiratory support to be implemented to help as much patient as possible and ensure patient received the respiratory support level needed, hence the need to understand use case and efficacy of Non-invasive respiratory support strategies.

Respiratory failure is the inability of the respiratory system to perform one or both of its main functions, the first is to provide oxygen for metabolism and the other is to remove carbon dioxide created from it. From this definition we usually divide respiratory failure into type 1 (hypoxemic) and type 2 (hypercapnic) respiratory failure. Acute respiratory failure can be life threatening because sudden derangement of arterial blood gases and acid-base status can disrupt vital metabolism while chronic respiratory failure usually produces indolent and slowly progressive clinical picture. Acute respiratory failure is a syndrome rather than a disease therefore the respiratory support provided must be tailored based on the disease causing it.[1]

In many cases, both respiratory failures can coexist. Disease that causes hypoxemia can be complicated by processes causing pump failure and hypercapnia. The opposite is also true. Although ARF is defined by content of arterial oxygen or carbon dioxide concentrations, the major threat to the patients is disruption of oxygen delivery to the tissue which can disrupt metabolism and many homeostasis processes.[1]

NON-INVASIVE STRATEGY FOR ACUTE RESPIRATORY FAILURE

Securing the airway is the most important component in the management of ARF hence the popularity of invasive mechanical ventilation (IMV). There are several disadvantages of IMV namely the need to insert endotracheal tube (ETT) which is technically challenging and potentially can create another infectious problem such as Ventilator-associated

pneumonia (VAP) and accompanying complication such as sepsis or septic shock. This disadvantage is profoundly encountered in the group of patients who already develop signs of respiratory failure but who still have intact airway reflexes and didn't have excessive secretions so that they are able to protect their own airways. This group of patients will benefit greatly from non-invasive strategies by avoiding intubation.[2]

Non-invasive respiratory support encompasses several different devices such as Non-invasive ventilation (NIV) also known as Bi-level positive airway pressure (Bi-PAP), continuous positive airway pressure (CPAP) and High flow nasal Oxygen (HFNO). There have been several guidelines describing their use case and level of evidence of their usefulness, for example NIV strongest evidence is in Acute exacerbation of chronic obstructive respiratory disease (AECOPD) and acute cardiogenic pulmonary edema while its evidence in acute hypercapnic respiratory failure due to obesity, neuromuscular disease, chest wall deformity is weaker[3]. CPAP and HFNO are most likely more useful in hypoxemic respiratory failure case.[4]

Delivery of NIV can be done in different settings from emergency room, medical ward, high care unit (HCU) and intensive care unit (ICU) although trained staff and appropriate monitoring system should be in place. This is due to failure of NIV is still about 20-30% therefore patient selection and the severity of respiratory failure when NIV was initiated will determine the successful outcome.[5] CPAP can also be delivered from the same machine of NIV/Bi-PAP. On the other hand, HFNO while also best deployed in place with monitoring systems but has advantages in simpler setup, maintenance, training, and monitoring. It also tend to be better tolerated by patient due to its nasal prong interface and warm and humidified flow of oxygen it produce.[5,6]

PHYSIOLOGY OF NON-INVASIVE RESPIRATORY SUPPORT STRATEGIES

Respiratory disorder could create distortion in lung compliance, the amount of pressure required to expand the lung. This pressure is known as transpulmonary pressure (TPP) which is expressed as alveolar pressure minus pleural pressure. Both increase and decrease in lung compliance can create difficulty in breathing. Increased compliance such as emphysema will make it harder for TPP to expand more volume into the lung because its already in high volume during rest. Decreased compliance such as acute cardiogenic pulmonary edema or acute respiratory distress syndrome will also make it harder to expand lung due to resistive effect of air-filled alveoli.[7]

The provision of respiratory support through patient upper airway by mask or similar device and without using invasive means such as endotracheal tube is the definition of non-invasive ventilation. Usually Bi-level positive airway pressure (BPAP) is applied to keep airway secure.[5] Different pressure support will be delivered during inspiration and expiration namely Inspiratory positive airway pressure (IPAP) and Expiratory airway pressure (EPAP). This pressure difference will drive and augment ventilation for the patient.[8] Non-invasive ventilation reduces the work of breathing through several mechanisms. The generation of EPAP will prevent airway collapse thus reducing the initial work of initiating inspiration while IPAP will augment TPP therefore reducing main work of breathing load.[7]

On the other hand, CPAP provide continuous pressure support in the form of positive end expiratory pressure (PEEP) which is basically have the same effect as EPAP, but It doesn't support or augment patient tidal volume and minute ventilation. CPAP provide constant pressure support during inspiration and expiration therefore it create a pneumatic splint of the upper airway preventing it to collapse during sleep and prevent small airways from being collapsed during end expiration hence the improvement of oxygenation.[1]

High flow nasal oxygen can deliver high concentration oxygen with constant FiO2 and higher flow than conventional oxygen therapy, up to 60 L/minutes. The high flow can help wash out CO2 and the high concentration of oxygen will create oxygen reservoir in the upper airway, these will reduce dead space. Higher flow of oxygen can also create positive pressure in the upper airways and this can be transmitted to the small airways as PEEP thereby giving similar positive effect as CPAP on respiratory process although in smaller ways.[9]

ACUTE HYPERCAPNIC RESPIRATORY FAILURE

Acute Hypercapnic respiratory failure (AHCRF) is defined by PaCO2 > 45 mmHg with accompanying acidemia usually caused by defect in one or more respiratory pump component (CNS, peripheral nerves, respiratory muscles, and airway) causing insufficient ventilation to maintain normal PaCO2. Rapid elevation of PaCO2 as happened in acute event will result in drop of arterial Ph causing many metabolic disturbances. Most AHCRF is caused by acute exacerbation of COPD which NIV is standard treatment. However, there are other condition in which respiratory pump failure also causing AHCRF, so NIV is also used in wide ranging AHCRF etiologies such as cystic fibrosis, chest wall deformity, neuromuscular disease, and obesity/obesity hypoventilation syndrome. The use of NIV in these other etiologies is not as extensively researched as the use of NIV in AECOPD.[3,5]

The use of NIV in AECOPD patients with ARF is consistently shown to reduce mortality, prevent

intubation and reduce the risk of nosocomial pneumonia. The current ATS/ERS guideline recommended using NIV in AECOPD patient with pH ≤7.35, PaCO2 > 45 and respiratory rate >20-24 breath/minute despite adequate medical therapy. Within the range of pH indicated for NIV initiation, less severely ill patients with pH of 7.25-7.35 can benefit from NIV by resolving acidosis, prevent endotracheal intubation and invasive mechanical ventilation (IMV). The more severely ill patient with pH < 7.25 can benefit from NIV not to prevent intubation but as alternative to intubation and IMV. There is no absolute lower limit of pH in which NIV is contraindicated. However, more severe acidosis requires close monitoring and immediate access to intubation and IMV. However the use of NIV in patients with hypercapnia but without acidosis is not recommended because there is no significant improvement compared to conventional oxygen and standard medical treatment.[5,10,11]

Initiation of NIV compared to IMV in AECOPD has yielded better outcome for patient by reducing mortality and hospital length of stay. However, the need for NIV in AECOPD itself is a poor prognostic factor for 1 year and year mortality risk. Garcia-Sanz et al reported 1 year mortality risk of 26.2%- and 5-year mortality risk of 64.3%. This is because patient who need NIV usually older, have more severe COPD and complicated comorbidity.[11,12] Successful NIV as an alternative to IMV have added benefit to reduce rate of NIV is still significant and reported to be about 20-30%. This emphasizes the need for correct patient selection, timing, interface used, environment where NIV is being used and standardized predictor for NIV failure (table 1). Failure of NIV is associated with higher mortality and longer stay in intensive care unit. Several predictors for NIV failure are higher APACHE II score (>20.5)[13] at presentation and persistent hypercapnia and/or acidosis. Whenever possible the possibility of failure need to be considered as to withdraw NIV and replace it with IMV or to allow more conservative approach (not using NIV) if palliation is the preferred outcome.[11]

High flow nasal Oxygen (HFNO) can be considered as an alternative to NIV by virtue of its capability to provide constant FiO2, generation of positive airway pressure up to 7 cmH2O and provide humidified and warmed inspired air which can improve mucociliary clearance.[9,14] Xu et al conducted a meta-analysis of 10 study comprises of 1265 patients with hypercapnic respiratory failure. The use of HFNO compared to NIV resulted in comparable mortality, the need for IMV and ABG improvement with added benefit of comfortability and reduced side effects. However, HFNO patient with pH < 7.30 will most likely needed crossover or rescue therapy with NIV and these patients will need longer interval with NIV although the rate of intubation is similar. Additionally this study also showed that HFNO can reduce the need for NIV in stable hypercapnic patients without acidosis compared with conventional oxygen therapy.[14]

Although HFNO is not a first-line treatment for AHCRF, its use can be considered in AECOPD patients not severe enough to warrant NIV i.e.,

Correct Patient
• Strong evidence for NIV/BPAP • COPD exacerbation with hypercapnia • Cardiogenic pulmonary edema • Immunocompromised patient with ARF • Low-moderate certainty of evidence for CPAP and HFNO • Acute hypoxemic respiratory failure due to pneumonia, ARDS, COVID-19 • Alternative to NIV in hypercapnic respiratory failure
Correct timing
• Patient with Intact airway reflexes • NIV/BPAP : pH ≤7.35, PaCO2 > 45, RR > 20-24 despite standard therapy • CPAP/HFNO : Hypoxemia despite optimal conventional oxygen therapy
Correct termination
• Perform intubation if there is no improvement in clinical condition, pH, PCO2 or PO2 after 1-2 hours of application
Correct equipment and staff
• correct interface should be used and fit well enough • helmet interface should be considered in NIV/CPAP • The ward should have staff with proper training and proper monitoring equipment

Table 1. consideration for application of non-invasive strategies. cited from 3, 4, 5, 10, 19, 20

ICU and hospital admission, incident of ventilator associated pneumonia and tracheostomy.

Despite the formal criteria for initiation of NIV and increasing familiarity of NIV outside ICU the failure

Patient with hypercapnia but not acidosis and for patients whose NIV is contraindicated. The main advantage of HFNO to NIV is patient tolerance because HFNO with its nasal prongs is more comfortable and allow for communication and feeding to be instituted. This is important because intolerance to NIV interface is one of the causes for NIV failure. HFNO might be also considered for purpose of filling in the break between NIV for feeding, medication or for patient with discomfort of NIV but still willing to continue NIV or for patient who outright decline NIV.[11,14,15]

Other causes of hypercapnic respiratory failure due to tuberculosis infection prevalent in Indonesia is non cystic fibrosis (CF) bronchiectasis. It is characterized by permanent distortion of the airways with inflammation and mucus plugging with clinical manifestation of chronic cough with productive sputum, breathlessness, and obstructive pattern on spirometry. Acute exacerbation resulting in respiratory failure is not uncommon with these patients and might give similar presentation as patient with AECOPD. Institution of intubation and IMV in this group of patients will have high mortality and morbidity. However, the use of NIV in non-CF bronchiectasis is not thoroughly studied and the data is still lacking.[16]

Phua et al conducted retrospective study of patients with bronchiectasis and found that NIV failure is happened in 1/3 of patients while Hadda et al conducted retrospective study of patients with non CF bronchiectasis who experienced acute respiratory failure. More than half (52.45%) have tuberculosis as the etiology of bronchiectasis, and all have hypercapnia and acidosis on arterial blood gas (ABG). Of note, the presence of COPD is not confirmed due to lack of spirometry data. Almost 2/3 of patients are successfully treated with NIV with notable findings of correction of pH and PCO2 parameters which comparable with those on IMV. The failure rate of these 2 retrospective studies is higher than NIV failure in AECOPD (20%) but still showed the feasibility of NIV as first line treatment in non-CF bronchiectasis patients with ARF. When given as first line treatment, NIV reduce mortality and length of stay at hospital. In case of NIV failure, there is no notable increase in mortality and length of stay at hospital.[16,17]

ACUTE HYPOXEMIC RESPIRATORY FAILURE

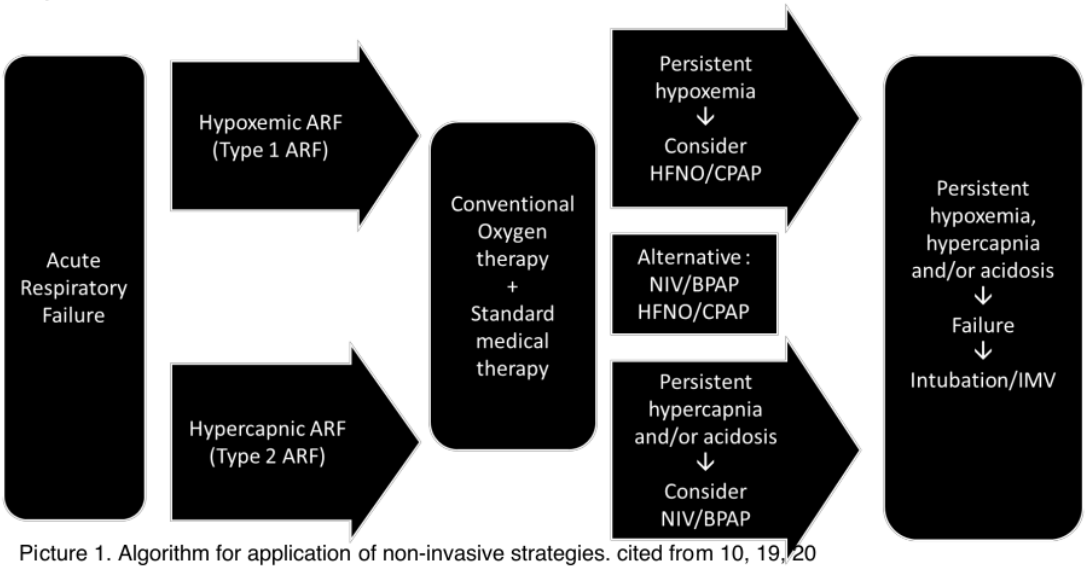
Acute Hypoxemic respiratory failure (AHORF) is defined by the arterial PaO2 < 60 mmHg and usually caused by several factors i.e., low inspired oxygen fraction, hypoventilation, ventilation/perfusion (V/Q) mismatch, shunt, or diffusion problem. De novo ARF is defined as respiratory failure without underlying chronic disease or pulmonary edema, most AHORF patients are part of this group, mainly represented by pneumonia and/or acute respiratory distress syndrome (ARDS). The use of NIV in this patient group is still controversial. This is due to the substantial difference in pathogenesis and physiological alteration which happened mainly not in respiratory pump but in alveoli, pulmonary vasculature and involving complex inflammatory process. Therefore NIV only has limited and specific use case i.e. in cardiogenic pulmonary edema and immunocompromised patients.[1,2,10]

Cardiogenic pulmonary edema causes hypoxemia by reducing lung compliance and increasing work of breathing due to congestion, hypercapnia sometimes can occur creating mixed respiratory failure. In patients not responding to standard medical treatment, application of positive pressure via mouth either using CPAP or NIV can reduce work of breathing and improve hypoxemia by reducing left ventricular preload and afterload. This beneficial effect is produced whether hypercapnia is present or not. Multiple trial has shown that NIV and CPAP can reduce the need for intubation and in hospital mortality. It also clarify that NIV/CPAP use in cardiogenic edema did not associated with myocardial infarction.[1,3,5,10]

Immunocompromised patients especially due to transplant and malignancy are often experiencing threat of ARF which require ICU treatment. The use of NIV and CPAP in this group with mild to moderate ARF can improve survival. Paula et al showed that in immunocompromised patient due to malignancy and transplant, NIV can reduce the need for intubation and improve survival. This effect is important for this group because IMV and further ICU treatment can have profound complications such as ventilator associated pneumonia. Although other study did not find reduction of intubation and mortality using NIV, ERS/ATS still recommended using early NIV/CPAP in immunocompromised patient with ARF because the benefit outweigh its undesirable effect.[10,18]

Lack of efficacy from NIV to reduce work of breathing in ARDS is in contrast with NIV efficacy in AECOPD. The use of NIV can reduce the work of breathing only after significant pressure support has been added. This large pressure will result in larger tidal volume which can exacerbate lung injury especially if prolonged thus the use of lung protective ventilation will be much more difficult with NIV. Gastric insufflation, air leaks and patient intolerance will also complicate the application of NIV. Therefore, IMV is the therapy of choice because it can be used to deliver low tidal volume ventilation consistently, reduce the work of breathing and can be used with total patient paralysis if needed.[10]

Failure of NIV in de novo ARF can be predicted early by higher severity score (APACHE II or SOFA), older age, pneumonia and/or ARDS as etiology and lack of improvement after 1 h. Another disadvantage of using NIV in this group is the risk of delaying intubation and poorer outcome due to NIV patient having larger tidal volume and develop more complication after switching to NIV. It was also shown that failure of NIV will worsen prognosis for de novo ARF therefore ERS/ATS did not make any recommendation for the use of NIV in de novo ARF. If the choice of using NIV is made with aim to prevent intubation then careful patient selection and sufficient precaution as not to delay intubation must be made.[10]



Picture 1. Algorithm for application of non-invasive strategies. cited from 10, 19, 20

Although IMV is the go-to strategy for ARF not responding to conventional oxygen therapy, sometimes circumstances and conditions didn't allow for it for example during pandemic. Non-invasive strategies have the potential to became bridge between conventional oxygen therapy and IMV in the hope that some of the patient can avoid intubation. Sakuraya et al found that in AHORF patients with etiology mainly of pneumonia, CPAP reduces short term mortality and has lower intubation rate compared to COT. Ferreyro et al also found that non-invasive strategies using helmet NIV and face mask NIV can reduce mortality and intubation rate while using high flow nasal oxygen is associated with decrease in intubation rate but not with mortality. Pitre et al also found that helmet CPAP may reduce mortality while HFNO may reduce the need for intubation.[4,19,20]

During COVID-19 pandemic discussion around the choices of non-invasive respiratory support strategies re-emerged due to abundance of AHORF cases due to COVID-19 pneumonia and ARDS. There is conflicting report on the merit of HFNO and NIV in preventing intubation and reduce mortality where some study reporting decrease in intubation rate and mortality while other study only reporting reduction in intubation rate or mortality but not both, or even reporting no significance at all. This difference can be explained by the difference in sample population characteristic, severity of disease and methodology used but this difference signaled that at least non-invasive oxygenation strategy is better than COT and can somewhat reduce the burden of IMV and mortality if used in selected population.[21]

Results from these meta-analysis and most other study are encouraging but need to be viewed with caution due to low certainty of evidence. Therefore, the use of non-invasive strategy needs to be used selectively, monitored carefully and IMV should be ready to deploy in case worsening condition occurs (picture 1).

CONCLUSION

Noninvasive oxygenation strategies such as NIV, CPAP and HFNO can be used effectively in selected groups of patients with acute hypercapnic and/or acute hypoxemic respiratory failure. It can reduce the need for intubation and IMV, lower mortality and hospital length of stay if used correctly. This represent huge untapped potential in the management of acute respiratory failure especially in Indonesia where its use is still limited mostly in intensive care settings.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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