Outcomes of Noninvasive Ventilation in Acute Hypoxemic Respiratory Failure in a Respiratory Intensive Care Unit in North India

Ritesh Agarwal MD DM, Ajay Handa MD DM, Ashutosh N Aggarwal MD DM, Dheeraj Gupta MD DM, and Digamber Behera MD

OBJECTIVES: To determine the outcomes of noninvasive ventilation (NIV) and the factors associated with NIV failure in patients with acute hypoxemic respiratory failure (AHRF). METHODS: This was a prospective observational study and all patients with AHRF requiring NIV over a one-and-a-half-year period were enrolled in the study. We recorded the etiology of AHRF and prospectively collected the data for heart rate, respiratory rate, arterial blood gases (pH, P_{aO_2}, P_{aCO_2}) at baseline, 1 hour, and 4 hours. The patients were further classified into 2 groups, based on the etiology of AHRF: either acute lung injury/acute respiratory distress syndrome [ALI/ARDS], or AHRF due to other causes. The primary outcome was the need for endotracheal intubation during the ICU stay. RESULTS: During the study period, 287 patients were admitted in the ICU, and of these 40 (13.9%) (21 ALI/ARDS, 19 AHRF due to other causes; 16 male, 24 female patients; mean ± SD age 43.2 ± 20.6 years) patients with AHRF were initiated on NIV. The baseline characteristics were similar in the 2 groups. After 1 hour there was a significant decrease in respiratory rate and heart rate, with increase in pH and P_{aO_2}; however, there was no difference in improvement of clinical and blood-gas parameters between the 2 groups. The NIV failures, the mean ICU and hospital stay, and the hospital mortality were similar in the 2 groups. In the univariate logistic regression model the only factor associated with NIV failure was the baseline ratio of P_{aO_2} to fraction of inspired oxygen (P_{aO_2}/F_{IO_2}) (odds ratio 0.97, 95% confidence interval 0.95–0.99). CONCLUSIONS: NIV should be judiciously used in patients with AHRF. A low baseline P_{aO_2}/F_{IO_2} ratio was associated with NIV failure. *Key words: noninvasive ventilation, acute hypoxemic respiratory failure, continuous positive airway pressure, CPAP, bi-level positive airway pressure, pneumonia, acute lung injury, ALI, acute respiratory distress syndrome, ARDS.* [Respir Care 2009;54(12):1679–1687. © 2009 Daedalus Enterprises]

Introduction

Noninvasive ventilation (NIV) has revolutionized the management of diverse causes of acute respiratory failure (ARF). It not only avoids the need for endotracheal intubation but also reduces the occurrence of complications such as nosocomial infection, and decreases intensive care unit (ICU) stay and overall cost of hospitalization in selected patients.[1] In NIV, 2 different pressures are used (an inspiratory pressure and an expiratory pressure), whereas continuous pressure maintains one constant pressure throughout the respiratory cycle. Theoretically, NIV may confer an advantage over continuous positive airway pressure, by reducing the work of breathing during inspiration, by providing additional inspiratory pressure. In hypercapnic respiratory failure secondary to chronic obstructive pulmonary disease (COPD), the use of NIV is associated with reduced tracheal intubation, duration of hospitaliza-

Ritesh Agarwal MD DM, Ajay Handa MD DM, Ashutosh N Aggarwal MD DM, Dheeraj Gupta MD DM, and Digamber Behera MD are affiliated with the Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh, India.

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Correspondence: Ritesh Agarwal MD DM, Department of Pulmonary Medicine, Postgraduate Institute of Medical Education and Research, Chandigarh 160012, India. E-mail: riteshpgi@gmail.com.

tion, and mortality, and NIV has become the standard of care in this setting.[2-6] The application of NIV in acute hypoxemic respiratory failure (AHRF) has been an area of research over the last 2 decades.[7] Two recent meta-analyses did not find any strong evidence to support the role of NIV in AHRF and acute lung injury/acute respiratory distress syndrome (ALI/ARDS).[8,9] However, in a few randomized controlled trials of NIV in AHRF (pneumonia in immunocompromised hosts and after lung-resection surgery), NIV was found to reduce the need for intubation and even mortality.[10-12] In AHRF due to cardiogenic pulmonary edema, use of NIV has been shown to reduce mortality in meta-analysis,[13] but a recent large trial failed to demonstrate any survival advantage.[14]

In many patients, application of NIV does not obtain adequate ventilation, and eventually endotracheal intubation and invasive ventilation are required for the management of ARF. The failure rate of NIV ranges from 5% to 50%, depending on the etiology and severity of ARF.[3,4,15-18] Also, some patients will initially benefit from NIV (for hours to a few days) but will then deteriorate and require intubation.[19] Failure to identify the patients who are likely to fail NIV can cause inappropriate delay of intubation, and can lead to clinical deterioration and increased morbidity and mortality.[16] It is important to ascertain the factors associated with NIV failure so that we can identify the high-risk patients likely to fail NIV. This subject of NIV in AHRF has been widely researched, with abundant data published from the developed world,[10,15,18,20-28] but hardly any data from India.

We have recently described the factors predicting effectiveness of NIV in patients with COPD.[29] The aim of this study is to evaluate the NIV outcomes and identify potential risk factors of NIV failure in AHRF in a respiratory ICU.

Methods

Study Design and Patient Selection

This was a prospective observational study conducted in the respiratory ICU of the Postgraduate Institute of Medical Education and Research, Chandigarh, India. All patients requiring NIV for ARF between July 2004 and December 2005 were enrolled in the study. The study was cleared by the institute ethics committee, and written consent was obtained from all patients or the next of kin. Patients were included in the study if they met the definition of AHRF defined by the presence of both of the following criteria: clinical signs and symptoms of acute respiratory distress (dyspnea, respiratory rate more than 30 breaths/min, use of accessory muscles of respiration, presence of paradoxical breathing), and arterial blood gas (ABG) analysis with ratio of P_{aO_2} to fraction of inspired oxygen (P_{aO_2}/F_{IO_2}) less than 300 mm Hg (or P_{aO_2} less than 60 mm Hg) while the patient was breathing oxygen through an air-entrainment mask. Patients were excluded from the study if they met any of the following criteria: hypercapnia (P_{aCO_2} more than or equal to 45 mm Hg); respiratory arrest with need for immediate endotracheal intubation; multiple organ dysfunction; medically unstable condition (eg, hypotension, uncontrolled cardiac ischemia/arrhythmia); inability to protect airway (excess secretions, stuporous, or comatose patient); abnormalities that precluded proper fit of the interface (agitated or uncooperative patient, facial trauma or burns, facial surgery, or facial anatomical abnormality).

The following criteria were used for diagnosis of various causes of AHRF:

- ALI/ARDS: acute onset, bilateral diffuse pulmonary opacities, no clinical evidence of left atrial hypertension
- Pneumonia: clinical symptoms and signs of pneumonia and consolidation on chest radiograph
- Asthma: clinical symptoms suggestive of asthma and diffuse wheeze on chest auscultation
- Interstitial lung disease: clinical symptoms and signs suggestive of interstitial lung disease, with reticulonodular opacities on chest radiograph
- Post-extubation respiratory failure: development of AHRF following extubation not explained by any other cause

Noninvasive Ventilation

NIV was administered with the use of a portable noninvasive ventilator (VPAP II, ResMed, Sydney, Australia). The detailed procedure of NIV was explained to the patient for improving compliance. NIV was delivered to patients in bed, at an angle of 30–45°, and in all patients a full face mask (UltraMirage, ResMed, Sydney, Australia) was used as an interface for delivery of NIV. At the outset the patient was started on an inspiratory pressure of 8 cm H_2O and expiratory pressure of 4 cm H_2O. The inspiratory and expiratory pressure were titrated in increments of 2 cm H_2O, based on continuous pulse oximetry (to achieve arterial oxygen saturation [measured via pulse oximetry] of 92%); arterial blood gases (at 1 hour and 4 hours, and periodically thereafter as clinically indicated); subjective alleviation of patient's dyspnea; decrease in respiratory rate; and good patient-ventilator synchrony; or until a maximum inspiratory pressure of 20 cm H_2O and expiratory pressure of 10 cm H_2O was reached.

Oxygen supplementation was provided through a port in the mask, to keep arterial oxygen saturation more than 92%. The presence of air leaks was frequently assessed,

and the patient was constantly encouraged and reassured. The NIV was applied continuously for as long as possible in the first 24 hours. Patients were allowed intermittent periods off the NIV, for eating or expectoration of secretions, and during that period they were given oxygen through an air-entrainment mask, with F_{IO_2} of 0.5. Weaning from NIV was done by reducing the duration of NIV to 6–8 hours per day. At that point, if the respiratory rate remained below 25 breaths/min and P_{aO_2} was above 60 mm Hg without any ventilatory support, NIV was definitively withdrawn. Appropriate medical therapy was administered in addition to NIV, as required.

End Points and Definitions

The demographic details of patients were recorded, which included age, sex, body mass index, etiology of AHRF, and the presence and absence of associated comorbid illnesses. The disease severity was calculated using the Acute Physiology and Chronic Health Evaluation (APACHE II) scores. We collected the data for heart rate, respiratory rate, arterial blood gases (pH, P_{aO_2}, and P_{aCO_2}) at baseline, 1 hour, and 4 hours. The primary outcome was NIV failure, defined as the need for endotracheal intubation during the ICU stay. Generally, the following criteria indicated the need for tracheal intubation: inability to improve or stabilize gas exchange, or dyspnea in 1 hour; failure to improve agitation from hypoxemia or changes in mental status linked to respiratory impairment; bradycardia (heart rate $<$ 60 beats/min with altered mental status); hypotension (systolic blood pressure $<$ 90 mm Hg); respiratory arrest; failure to maintain $S_{pO_2} \geq 88\%$; significant metabolic and/or respiratory acidosis (pH $\leq$ 7.20). Ultimately, clinical judgment was applied in the decision to intubate any patient, and was left to the intensivist's clinical judgment. We also noted the patient outcomes in terms of the time spent on NIV, time to intubation, ICU stay, hospital stay, and hospital mortality.

Statistical Analysis

Statistical analysis was performed (SPSS version 10, SPSS, Chicago, Illinois). Statistical significance was assumed at a *P* value of less than .05. Results are presented in a descriptive fashion as number (percentage), mean ± standard deviation, or median and interquartile range. The differences between means of continuous and categorical variables were analyzed using the Mann-Whitney U and chi-square test, respectively. Improvements in clinical (respiratory and heart rate) and arterial blood gas parameters (pH, P_{aO_2}, and P_{aCO_2}) were analyzed using multifactorial repeated-measures analysis of variance with Bonferroni adjustment for multiple comparisons; the within-groups factor was time (zero, 1 hour, and 4 hours), and the between-groups factor was the diagnosis of AHRF (ALI/ARDS vs other causes), the intubation status (intubated vs not intubated), and the 2 factors together. A multifactorial analysis of variance with Bonferroni adjustment for multiple comparisons was used for studying the outcomes of the 2 diagnosis groups in intubated versus non-intubated patients with AHRF. Survival curves were constructed to study the time to intubation in patients failing NIV, using Kaplan-Meier analysis. Univariate logistic regression analysis was performed to derive crude odds ratios and 95% confidence intervals to analyze the factors associated with failure of NIV (ie, requirement of endotracheal intubation). The following variables were included: APACHE II scores, host immune status, baseline P_{aO_2}/F_{IO_2} ratio, improvement in respiratory rate and P_{aO_2} in the first hour and 4 hours after application of NIV, and etiology (ALI/ARDS vs other causes of AHRF).

Table 1. Respiratory ICU Admissions and Etiologies of Acute Hypoxemic Respiratory Failure Requiring Noninvasive Ventilation During the Study Period

	n (%)
Total Admissions to the respiratory ICU	287 (100)
Invasive ventilation	
Hypoxemic	98 (34.1)
Hypercapnic	70 (24.4)
Noninvasive Ventilation	
Hypoxemic	40 (13.9)
Hypercapnic	53 (18.5)
Oxygen therapy alone	26 (9.1)
Etiologies of AHRF Requiring NIV	
Pulmonary ARDS	18 (45.0)
Extrapulmonary ARDS	3 (7.5)
Interstitial lung disease	7 (17.5)
Pneumonia	5 (12.5)
Cardiogenic pulmonary edema	3 (7.5)
Acute severe asthma	3 (7.5)
Post-extubation respiratory failure	1 (2.5)

ICU = intensive care unit
AHRF = acute hypoxemic respiratory failure
NIV = noninvasive ventilation
ARDS = acute respiratory distress syndrome

Results

During the study period 287 patients were admitted in the respiratory ICU (Table 1). Of the 138 patients with AHRF, 98 required immediate endotracheal intubation. Forty (28.9%) patients with AHRF met the inclusion criteria and were initiated on NIV. The most common diagnosis of AHRF requiring initiation of NIV was ALI/ARDS (see Table 1). Other causes included interstitial lung disease, pneumonia, and others. There were 16 male and 24

Table 2. Baseline Characteristics of Patients With Acute Respiratory Failure, Stratified by Etiology

	ALI/ARDS (n = 21)	Other Etiologies (n = 19)	Total (n = 40)	P
Age (mean ± SD y)	41.5 ± 23.9	45.1 ± 16.6	43.2 ± 20.6	.31
Female (n, %)	12 (57.1)	12 (63.2)	24 (60.0)	.76
BMI (mean ± SD kg/m^2)	21.5 ± 3.7	23.3 ± 4.5	22.3 ± 4.1	.17
Underlying immunosuppression* (n, %)	9 (42.9)	10 (52.6)	19 (47.5)	.75
APACHE II score (mean ± SD)	14.9 ± 2.9	14.8 ± 5.1	14.9 ± 3.9	.71
Respiratory rate (mean ± SD breaths/min)	48.3 ± 9.1	46.2 ± 8.8	47.3 ± 8.9	.48
Heart rate (mean ± SD beats/min)	119.1 ± 16.5	123.3 ± 19.6	121.1 ± 17.9	.43
pH (mean ± SD)	7.42 ± 0.06	7.43 ± 0.07	7.43 ± 0.06	.55
P_{aO_2}/F_{IO_2} (mean ± SD)	131.2 ± 45.7	118.1 ± 46.9	125.1 ± 46.2	.30
P_{aCO_2} (mean ± SD mm Hg)	32.2 ± 7.3	32.3 ± 7.7	32.3 ± 7.4	.88

* Glucocorticoid therapy, cytotoxic drugs, neutropenia, hematologic malignancy, uncontrolled diabetes mellitus
ALI = acute lung injury
ARDS = acute respiratory distress syndrome
BMI = body mass index
APACHE = Acute Physiology and Chronic Health Evaluation
F_{IO_2} = fraction of inspired oxygen

female patients, with a mean ± SD age of 43.2 ± 20.6 years. The baseline demographics (age, sex, body mass index, and immunosuppressive status), clinical features (respiratory rate, heart rate, APACHE II scores), and arterial blood gases were similar in patients with ALI/ARDS and other causes of AHRF (Table 2).

The serial clinical and arterial blood gas parameters are shown in Table 3. After 1 hour there was a significant improvement in clinical (decrease in respiratory rate and heart rate) and blood gas (increase in pH and P_{aO_2} levels) parameters in patients managed with NIV. At 4 hours there was a decrement in respiratory rate and heart rate, but no difference in pH, P_{aO_2}, and P_{aCO_2} levels (see Table 3). There was no difference in improvement of clinical and blood gas parameters between the 2 groups of AHRF (see Table 3). Overall NIV was successful in 52.5% of patients with AHRF, with 12 (57.1%) of 21 patients in the ALI/ARDS group, and 7 (36.8%) of 19 patients in AHRF due to other causes group, respectively, requiring endotracheal intubation and invasive ventilation. Figure 1 depicts the time to endotracheal intubation. The respiratory, hemodynamic, and blood gas parameters of the patients requiring endotracheal intubation prior to intubation are shown in Table 4.

The mean ± SD inspiratory/expiratory pressure administered was 15.3 ± 3.1 cm H_2O/6.1 ± 1.8 cm H_2O, and was administered for a mean duration of 67.6 hours (Table 5). The mean duration for NIV failures requiring intubation was 17 hours (95% confidence interval 10.6–23.4 hours). Seven of the 12 patients requiring invasive ventilation in the ALI/ARDS group died, whereas 6 of the 7 patients in the AHRF-from-other-causes group died due to multiple organ dysfunction. The ICU and hospital stay was found to be similar in the 2 groups (see Table 5).

Univariate logistic regression analysis was performed to assess the factors associated with NIV failure (ie, endotracheal intubation). The only factor associated with failure of NIV was the baseline P_{aO_2}/F_{IO_2} ratio (odds ratio 0.97, 95% confidence interval 0.95–0.99) (Table 6).

Discussion

The results of this study show that application of NIV is associated with an initial improvement in gas exchange, and its application can avoid intubation in almost 53% of patients with AHRF. In the univariate analysis, only the severity of AHRF, as determined by baseline P_{aO_2}/F_{IO_2} ratio, was associated with failure of NIV. We were able to use NIV in 29% of admissions with AHRF, which reflects the fact that only a minority of patients with AHRF can receive NIV. The role of NIV in etiologies of AHRF such as pneumonia, asthma, and ALI/ARDS is controversial, and controlled trials for the use of NIV in exacerbations of obstructive sleep apnea, bronchiectasis, and diffuse parenchymal lung diseases are lacking. Similarly, there is no role for NIV in patients with post-extubation failure, except as a preemptive therapy in high-risk patients (for re-intubation) following extubation.[30] This fact was also reflected in this study, with an almost 42% failure rate with NIV in AHRF. A recent French audit also suggested the benefit of NIV only in cardiogenic edema and COPD exacerbations, and not in de novo etiologies of ARF.[19] This point is further reflected in a recent study in which the failure rate of NIV for AHRF was as high as 60%.[31] International comparison of ICU data could be of great value. However, there is a paucity of data from India on the use of NIV in ARF. In fact, apart from our recent

Table 3. Serial Clinical and Arterial Blood Gas Parameters During the Intensive Care Unit Course of the 2 Groups Receiving NIV*

	AHRF From ALI/ARDS (n = 21)						AHRF From Other Etiologies (n = 19)					
	Intubated (n = 12)			Not Intubated (n = 9)			Intubated (n = 7)			Not Intubated (n = 12)		
	0 h	1 h	4 h	0 h	1 h	4 h	0 h	1 h	4 h	0 h	1 h	4 h
Respiratory rate (breaths/min)	51.6 ± 8.8	44.3 ± 9.0[a]	43.6 ± 8.5[b]	44 ± 8.0	32.7 ± 7.5[a]	29.7 ± 4.2[b]	48 ± 9.7	38.3 ± 9.1[a]	32.1 ± 10.0[b]	45.2 ± 8.5	35.6 ± 6.1[a]	33.3 ± 5.8[b]
Heart rate (beats/min)	121.5 ± 17.2	114.8 ± 19.0[a]	111.8 ± 18.8[b]	115.8 ± 16.0	104.9 ± 11.0[a]	97.3 ± 8.9[b]	127.4 ± 19.6	112 ± 19.2[a]	110 ± 24.8[b]	120.8 ± 20.0	109.6 ± 18.7[a]	104.4 ± 15.6[b]
pH	7.41 ± 0.05	7.41 ± 0.07	7.41 ± 0.14	7.44 ± 0.07	7.45 ± 0.05	7.46 ± 0.05	7.43 ± 0.07	7.43 ± 0.06	7.43 ± 0.06	7.42 ± 0.07	7.44 ± 0.06	7.43 ± 0.07
P_{aO_2} (mm Hg)	57.5 ± 26.7	76.9 ± 22.5[e]	74.8 ± 24.6	66.7 ± 19.1	94.9 ± 36.6[e]	87.8 ± 22.6	44.7 ± 15.8	59.4 ± 15.2[e]	51.1 ± 12.0	60.9 ± 16.7	86.2 ± 35.0[e]	86.5 ± 28.7
P_{aCO_2} (mm Hg)	33.1 ± 7.8	32.9 ± 6.3	34.3 ± 7.0	31.1 ± 6.8	31.6 ± 3.2	32.2 ± 3.3	34.0 ± 5.0	33.6 ± 6.4	36.4 ± 7.8	31.4 ± 8.9	32.2 ± 7.6	33.3 ± 7.2
Inspiratory pressure (cm H_2O)	6.8 ± 1.0	11.8 ± 1.7[a,e]	15.8 ± 3.7[b]	6.9 ± 1.1	10.3 ± 1.4[a,e]	14 ± 2.6[b]	6.9 ± 1.1	12.7 ± 1.8[a,e]	17.0 ± 1.9[b]	6.8 ± 1.0	10.7 ± 1.8[a,e]	14.8 ± 2.9[b]
Expiratory pressure (cm H_2O)	3.9 ± 0.9	5.3 ± 0.9[a]	6.1 ± 1.4[b]	4.2 ± 1.0	5 ± 0.7[a]	5.4 ± 1.0[b]	4.1 ± 1.1	5.6 ± 0.8[a]	6.9 ± 1.6[b]	4.1 ± 1.1	5.5 ± 1.2[a]	6.3 ± 1.7[b]
Oxygen flow (L/min)	9.5 ± 1.7	11.8 ± 1.6[a]	15 ± 0[b,f]	8.4 ± 2.1	10.3 ± 2.6[a]	13 ± 3.5[b,f]	9.9 ± 0.4	11.9 ± 0.4[a]	15.0 ± 0[b,f]	6.3 ± 2.5	8.1 ± 2.8[a]	10.1 ± 3.4[b,f]

* All values are mean ± SD.
a = value at 1 h significantly different from that at baseline within the groups
b = value at 4 h significantly different from that at 1 h within the groups
c = value at 1 h significantly different from that at baseline between the diagnosis groups
d = value at 4 h significantly different from that at 1 h between the diagnosis groups
e = value at 1 h significantly different from that at baseline between the intubation groups
f = value at 4 h significantly different from that at 1 h between the intubation groups
g = value at 1 h significantly different from that at baseline between the diagnosis and intubation groups
h = value at 4 h significantly different from that at 1 h between the diagnosis and intubation groups
NIV = noninvasive ventilation
AHRF = acute hypoxemic respiratory failure
ALI = acute lung injury
ARDS = acute respiratory distress syndrome

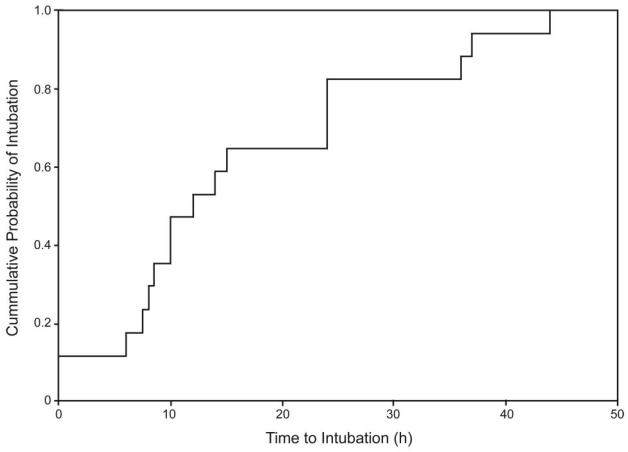

Fig. 1. Kaplan-Meier curve of the probability of endotracheal intubation over time in the 19 patients failing noninvasive ventilation. Most intubations occurred in the first 24 hours.

study,[29] there are only 2 published studies that have investigated the use of NIV in patients with ARF.[32,33]

In contrast to the vast body of literature that has established the role of NIV in COPD with ARF,[5,34] the role of NIV in AHRF is still an area of controversy.[8,9,35,36] Although there is a strong pathophysiological basis for the role of NIV in AHRF,[37] the evidence on the role of NIV in AHRF does not support its routine use. A variety of reasons have been put forth to explain this paradox. The syndrome of AHRF represents a group of heterogeneous etiologies of variable severities and, not surprisingly, the benefits of NIV in this syndrome have been varied. In fact, for similar degrees of hypoxemia the outcome of NIV depends on the underlying pathophysiologic mechanisms responsible for AHRF.[16] In a study that recruited patients with pneumonia and cardiogenic pulmonary edema and similar severity of hypoxemia, it was shown that the outcomes of patients with pneumonia were worse, compared to cardiogenic pulmonary edema, despite an initial analogous improvement in oxygenation between the 2 groups.[38]

An important predictor of NIV failure has been the severity of the underlying illness, as assessed with the APACHE II score or similar scoring systems,[15,17,18,24,39,40] although some studies have failed to demonstrate this observation.[41-43] In our study, the baseline APACHE II score was not associated with NIV failure. A probable reason for this is the fact that the APACHE II score itself was not very high in our patients, as we excluded patients with shock. In patients with AHRF, the presence of ALI/ARDS is recognized as an important cause of NIV failure.[15,24,44] The failure rate of NIV in ALI/ARDS is very high, and was reported as almost 51% in a large multicenter study, in contrast to 10% and 18% failure rates, respectively, in cardiogenic pulmonary edema and pulmonary contusion.[15] In the present study the diagnostic profile of patients with AHRF included ALI/ARDS as the commonest cause, and, specifically, ALI/ARDS was associated with a 57% failure rate (12 of 21 patients with ALI/ARDS in this study failed NIV trial).

There was significant improvement in clinical and blood gas values with the use of NIV in both the groups. The baseline P_{aO_2}/F_{IO_2} ratio, but not the improvement in oxygenation at 1 hour, was associated with NIV failure in this study, in contrast to other studies.[15,18] In patients with AHRF, an initial transient improvement in the clinical and blood gas parameters does occur with NIV, but the underlying process, such as sepsis or pneumonia, takes at least 24–48 hours to improve with antibiotics and other supportive measures. This leads to late NIV failures despite an improvement in the early hours.[15,31,38,40,45] Also there are a subset of patients who initially seem to respond to NIV but then fail to improve, and this cohort of patients are termed as "late NIV failures."[40,45] In patients with late NIV failure the improvement in clinical parameters and arterial blood gases does not predict successful outcome with NIV.

Numerous studies have investigated the role of NIV in AHRF. In patients with hypoxemic respiratory failure, NIV is as effective as conventional ventilation in correcting gas exchange.[46] In several studies the presence of multiple organ dysfunctions, shock, and severity of illness, as determined by ICU severity score, have predicted failure of NIV.[18,22,26] In a large multicenter study, Antonelli et al showed that Simplified Acute Physiology Score II more than or equal to 35, ALI/ARDS, pneumonia as the etiology of AHRF, P_{aO_2}/F_{IO_2} ratio after 1 hour of NIV $\leq$ 146 mm Hg predicted NIV failure.[15] In a case-control study, the use of NIV was associated with lesser intubation rates, and cardiogenic pulmonary edema and ALI/ARDS were factors associated with lower and higher risk respectively for intubation.[24] In another large study involving patients with ALI/ARDS, Simplified Acute Physiology Score II more than or equal to 35, and P_{aO_2}/F_{IO_2} ratio after 1 hour of NIV $\leq$ 175 mm Hg predicted a higher likelihood of intubation.[18] This suggests that NIV is beneficial in selected patients with AHRF. The issue is the selection of the right patient who will benefit from NIV. Another important issue is the early identification of the patient who is failing NIV, so as to avoid the delay in intubation. Delays in endotracheal intubation in patients being managed with NIV have been shown to be associated with decreased survival.[47] It is important to select patients properly, as unselected patients (eg, ALI/ARDS with shock) have uniformly poor outcomes.[26] Also, the duration of the NIV trial requires close monitoring, and patients who do not respond to NIV should be intubated early, because the mortality risk increases with delays.

The major limitations of this study include the relatively small number of patients (although it is the largest number

Table 4. Respiratory, Hemodynamic, and Arterial Blood Gas Parameters Prior to Endotracheal Intubation in the 19 Patients Who Required Invasive Ventilation

	Mean	95% Confidence Interval	Median	Range
Respiratory rate (breaths/min)	41	38.8–43.2	42	34–50
Heart rate (beats/min)	133.2	126.2–140.1	135	110–155
Systolic blood pressure (mm Hg)	116.9	105.2–128.5	116	70–155
Diastolic blood pressure (mm Hg)	65.6	58.2–72.9	70	30–90
pH	7.22	7.18–7.25	7.2	7.1–7.31
P_{aO_2} (mm Hg)	62.3	58.3–66.3	60	51–82
P_{aCO_2} (mm Hg)	38.9	33.3–44.6	36	15–66
HCO_3 (mEq/L)	15.3	14.2–16.4	15	12–20

Table 5. Outcome Parameters During the Intensive Care Unit Course of the 2 Groups Receiving Noninvasive Ventilation

	AHRF From ALI/ARDS (n = 21)		AHRF From Other Etiologies (n = 19)	
	Intubated (n = 12)	Not Intubated (n = 9)	Intubated (n = 7)	Not Intubated (n = 12)
Inspiratory pressure (mean ± SD cm H_2O)	15.8 ± 3.7[b]	14 ± 2.6	17 ± 1.9[b]	14.8 ± 2.9
Expiratory pressure (mean ± SD cm H_2O)	6.1 ± 1.4	5.4 ± 1.0	6.9 ± 1.6	6.3 ± 1.7
Duration of NIV (mean ± SD h)	18.7 ± 15.6	82.3 ± 60.5[b]	17.9 ± 10.9	61.3 ± 32.7[b]
Mortality (n, %)	7 (58.3)	0	6 (85.7)	0
ICU stay (mean ± SD d)	10.2 ± 10.1	7.4 ± 4.4	9.9 ± 6.0	5.3 ± 2.4
Hospital stay (mean ± SD d)	14.6 ± 15.1	12 ± 4.7	12.3 ± 9.4	9.2 ± 5.4

a = value significantly different between ALI/ARDS and other diagnosis group
b = value significantly different between intubated and non-intubated group
c = value significantly different between intubated and diagnosis groups together
AHRF = acute hypoxemic respiratory failure
ALI = acute lung injury
ARDS = acute respiratory distress syndrome

Table 6. Univariate Analysis of Factors Predicting Failure of Noninvasive Ventilation

	NIV Success (n = 21)	NIV Failure (n = 19)	Crude Odds Ratio	95% Confidence Interval	P
ALI/ARDS (n, %)	7 (33.3)	12 (63.2)	0.44	0.12–1.6	.20
Underlying immunosuppression (n, %)	8 (38.1)	11 (57.9)	2.23	0.63–7.93	.21
APACHE II score (mean ± SD)	14.8 ± 4.4	15 ± 3.5	1.02	0.87–1.19	.85
Baseline P_{aO_2}/F_{IO_2} (mean ± SD mm Hg)	144.2 ± 48.6	103.8 ± 33.1	0.97	0.95–0.99	.01
Change in Respiratory Rate (mean ± SD breaths/min)					
Hour 0 to hour 1	–10.3 ± 4.7	–8.2 ± 4.9	1.04	0.95–1.13	.40
Hour 0 to hour 4	–12.9 ± 7.5	–10.9 ± 7.6	1.10	0.96–1.27	.17
Change in P_{aO_2} (mean ± SD mm Hg)					
Hour 0 to hour 1	17.7 ± 25.5	26.5 ± 31.6	0.99	0.97–1.01	.33
Hour 0 to hour 4	23.7 ± 26.1	13.3 ± 21.4	0.98	0.95–1.01	.18

NIV = noninvasive ventilation
ALI = acute lung injury
ARDS = acute respiratory distress syndrome
APACHE = Acute Physiology and Chronic Health Evaluation
F_{IO_2} = fraction of F_{IO_2}

of patient data published from India on the use of NIV in AHRF). Thus, many of the conclusions regarding risk factors in the logistic regression model of our study have limitations, as the small data set did not allow for a valid assessment of whether some of these conditions in the study population may or may not be a contributing factor

for success or failure of NIV. Another problem is the diagnosis of various causes of AHRF. Although we included definitions for various diagnostic categories, occasionally there could be problems in differentiating between various entities, such as pneumonia and interstitial lung disease, and both might be classified as forms of ARDS. This may partially explain the lack of differences found between the 2 groups, although the most clinically feasible diagnosis was considered in a particular clinical situation, and the diagnostic category was changed after all the investigative work-up was available. Currently, patients who require NIV are managed with critical-care ventilators, which are capable of better oxygen delivery (due to the presence of oxygen blender) and better patient monitoring.[48] However, when this study was performed, due to resource constraints, the respiratory ICU possessed only a portable noninvasive ventilator, which was used in this study. This could have also negatively influenced the study results.

Conclusions

In conclusion, the result of this study suggests a high failure rate of NIV in patients with AHRF, and NIV should be judiciously used in patients with AHRF. In resource-poor countries, where facilities of ICU care and ventilatory support cannot be afforded by the economically deprived sections of the population, NIV offers the advantages of ventilatory support with an advantage of reduced incidence of nosocomial pneumonia and reduced ICU stay and overall hospital costs. The only caveat is that cases must be chosen carefully and monitored closely to avoid delays in intubation and its adverse effects. In cases of AHRF, NIV must be applied early and patients monitored closely in an intensive-care setting, so that endotracheal intubation can be carried out without any delay.

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