Original article

Noninvasive ventilation in acute respiratory failure: a study of clinical outcome and correlates for success

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Abstract

Background: Noninvasive ventilation (NIV) is increasingly used for acute respiratory failure although its effectiveness is unclear. **Methods:** This study was conducted to analyse clinical outcome in patients with acute respiratory failure treated with NIV and to identify the determinants predicting success and failure of this technique. This prospective study included acute respiratory failure patients eligible for NIV admitted to Multidisciplinary Intensive Care Unit from August 2006 to September 2007. All patients received NIV using oronasal masks. Arterial blood gases, chest radiograph, duration of NIV, ICU and hospital stay were compared. NIV was considered successful or failed according to the need for endotracheal intubation. **Results:** A total of 41 patients were enrolled. NIV was successful in 26 (63.4%) patients while failed in 15 patients (36.6%). The overall mortality was 34.1%. Patients managed successfully with NIV showed a significant increase in PaO_2 at 1 and 6 h and their duration of ICU stay was shorter as compared to those who failed NIV. Changes in $PaCO_2$, pH and hospital stay were similar between the groups. **Conclusions:** An improvement in PaO_2 after 1-2 and 6 h of NIV is associated with a successful outcome. NIV when successful is associated with shorter ICU stay and failure is associated with high mortality. Effectiveness of NIV in improving PaO_2 in the initial hours could be used to predict whether the patients with acute respiratory failure could be successfully treated with NIV.

Keywords: Acute respiratory failure, Noninvasive ventilation

Introduction

Respiratory failure is commonly encountered in medical practice and mechanical ventilation has been the mainstay of its management. Invasive ventilation has been associated with various complications and in a select group of patients, noninvasive ventilation (NIV) is an attractive alternative. The role of NIV in the treatment of chronic obstructive pulmonary disease is well-established[1] and it is now being increasingly used in the treatment of acute respiratory failure due to various causes including acute asthma,[2] pulmonary oedema,[3] septic shock[4] and after abdominal surgery.[5] It is found to reduce incidence of endotracheal intubation and nosocomial pneumonia.[6,7] It is also useful in preventing reintubation in patients with postextubation respiratory distress.[8] The effectiveness of NIV in acute respiratory failure is not studied well.

In this study, an attempt has been made to analyse the clinical outcome in patients admitted with acute respiratory failure treated with NIV and also to identify the determinants which predict the success and failure of this technique.

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Methodology

A prospective, observational study of patients treated with NIV was conducted. The study period was from 1st August 2006 to 30th September 2007. All adult patients admitted in our Multidisciplinary Intensive Care Unit (MICU) with at least two of the symptoms of acute respiratory failure (PaO_2/FiO_2 < 200, $PaCO_2$ > 45 mm Hg with pH < 7.35, Respiratory rate (RR) ≥ 35 breaths/min, using accessory muscles of respiration and paradoxical breathing) were included in the study. Patients with apnoea, unconsciousness, haemodynamic instability, unco-operative behaviour, facial burns, facial trauma, copious secretions, those at high risk of aspiration, and those who received NIV for less than 1 hour were excluded. Approval of the institutional ethical committee was obtained for the study.

A total of forty five patients were screened of which forty one patients were enrolled and treated with NIV. Out of the four patients who were excluded, three patients were discharged against medical advice due to financial constraints and one patient had 'do not intubate' order (*Figure 1*) .

Thirty four patients received NIV through ResMed Sullivan® VPAP® II and seven through critical care ventilator (Evita ™ 2 Dura – Dräger Medical Inc., Lübeck, Germany). All patients were connected to oronasal masks (Mirage™ NV Full Face, RedMed) with minimal leak around the masks. Patients were treated with continous positive airway pressure (CPAP) mode, pressure support ventilation (PSV) mode or Bilevel positive airway pressure (BiPAP) modes of ventilation during the NIV trial as required. Initiation, maintenance and weaning of NIV were done jointly by the consultant intensivist and the respiratory therapists. In the critical care ventilator, FiO_2 was set to achieve a SpO_2 > 92% or a PaO_2 > 65 mm Hg whereas when VPAP II (ResMed) was used, oxygen flow was set to achieve a SpO_2 > 92% or a PaO_2 > 65 mm Hg. Arterial blood gases (ABG) were assessed immediately before (baseline) and during an initial 1 to 2 hour trial of NIV. NIV was discontinued and invasive ventilation commenced if respiratory distress increased or the patient required endotracheal intubation for any other reason. The

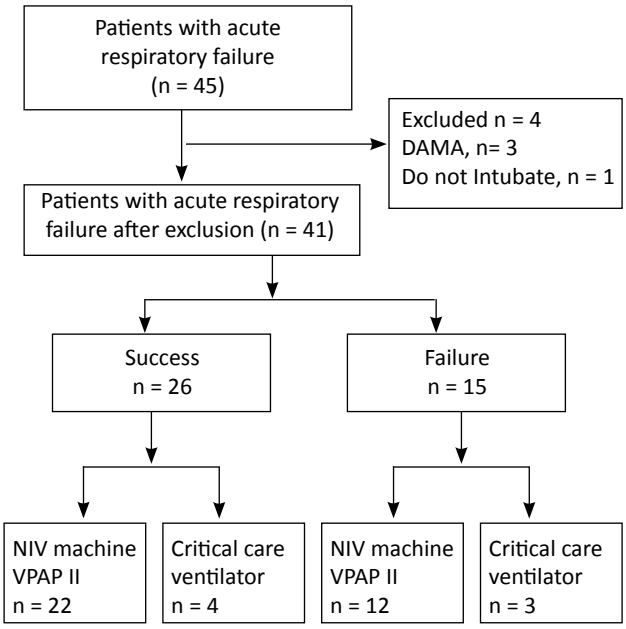

Figure 1 : Flow chart of the patients in the study
DAMA: Discharged against medical advice

patients had another ABG at 6 hours after NIV if they were not already intubated. Chest radiograph on first and third day of NIV, total duration of NIV treatment, MICU stay and total hospital stay were also recorded. A successful clinical outcome was defined as weaning from NIV and failure was defined as NIV use that eventually required endotracheal intubation and ventilation.

The primary outcome variables were the number of patients recovered with NIV, requirement for endotracheal intubation and mechanical ventilation at any time during the study and blood gas changes during the period of NIV. Secondary end points included development of nosocomial infections after study entry, duration of ventilatory assistance, length of ICU stay and survival of ICU and hospital admission.

Values are expressed as mean ± SD. We used Chi-square test for categorical variables and paired t test and repeated measures ANOVA for continuous variables. We conducted the statistical analyses with statistics software SPSS 11, SPSS, Chicago, Illinois. Differences were considered significant when p was < 0.05.

Results

A total of 41 patients admitted during 12-month period with acute respiratory failure from 1st August 2006 to 30th September 2007 were eligible for noninvasive ventilation. The demographic data of patients included in the study is given in (*Table 1*).

Table 1: Demographic data and type of respiratory failure.

	Success (n = 26)	Failure (n = 15)
Age*	45.3 ± 19.7	56.4 ± 17.1
Gender (M/F)*	13 / 13	7 / 8
Respiratory failure Type I Respiratory failure Type II	15 11	9 6

*P>0.05

Noninvasive mechanical ventilation was successful in 26 (63.4%) patients with acute respiratory failure. 15 patients (36.6 %) failed NIV, as defined by the need for endotracheal intubation. The overall mortality was 34.1% (14 out of 41 patients).

The type of respiratory failure had no association with success or failure of NIV (*Table 2*). The causes of respiratory failure did not largely differ between NIV success and failure but the data suggested that when respiratory illness was the primary cause of respiratory failure, the success rate of NIV is low (2/8, 25%). Respiratory illnesses were bronchial asthma, bronchiectasis, pleural effusion, acute respiratory distress syndrome and pulmonary oedema.

Table 2: Causes of respiratory failure and their frequency (n) in both groups

Diagnosis	Success	Failure
Infection (sepsis)	7	3
Primary respiratory illness	2	6
Surgery (postoperative)	9	2
Trauma	1	2
Malignancy	4	2
Other	3	0

The changes in arterial blood gases before, at 1 hour and after 6 hours of NIV trial are shown in (*Table 3*). An improvement in PaO_2 at one hour was seen to be associated with a successful outcome (p = 0.002, with 95% confidence interval, 28.32 - 112.8). The improvement in PaO_2 continued to be significantly higher after six hours (p = 0.001, with 95% confidence interval, 36.42- 125.26) in patients who were eventually weaned successfully with NIV alone. Changes in $PaCO_2$ and pH did not differ among the groups at both one and six hours of NIV.

Table 3: Arterial blood gases at baseline, 1 h and 6 h after NIV

		NIV Success n = 26	NIV Failure n = 15
PaO_2 (mm Hg)	Baseline*	76.7 ± 18.6	78.9 ± 10.7
	At 1 h**	107.7 ± 27.8	53.6 ± 27.4
	At 6 h***	103.5 ± 28.7	76 ± 17.6
$PaCO_2$ (mm Hg)	Baseline*	43.3 ± 17.1	53.8 ± 25.4
	At 1 h*	41.3 ± 14.9	51.2 ± 20.2
	At 6 h*	40.8 ± 13.4	51.1 ± 20.2
pH	Baseline*	7.36 ±0.9	7.28 ± 0.1
	At 1 h*	7.39 ± 0.6	7.33 ± 0.1
	At 6 h*	7.39 ± 0.05	7.31 ± 0.13
RR (bpm)	Baseline*	31 ± 9	33 ± 7
	At 1 h*	25 ± 7	28 ± 8
	At 6 h*	24 ± 7	28 ± 7

*P>0.05 ** P ≤0.002 *** P = 0.001

RR did not differ between the groups, either at baseline, one hour or six hours of NIV and thus were not indicative of success or failure of NIV. The baseline respiratory rate was 31 ± 9 and 33 ± 7 breaths/min, at 1 hour of NIV was 25 ± 7 and 28 ±

8 breaths/min and at 6 hours of NIV was 24 ± 7 and 28 ± 7 breaths/min in the NIV success group and NIV failed group respectively (*Table 2*).

The radiological changes after 48-72 h of NIV were also analysed for any association with outcome. The changes were assessed by a radiologist blinded to the patient condition. An improvement in chest X-ray had a positive predictive value. All the patients in whom an improvement in chest X-ray was noted, NIV was successful. No patient in the failed group showed any improvement in the chest X-ray. However, five patients in the success group had deterioration in chest X-ray.

Patients in the NIV success group were ventilated with NIV for a longer period of time as compared to the NIV failed group (2.7 ± 0.9 days *vs.* 1.6 ± 0.7 days). The duration of ICU stay was significantly shorter by 3.13 days (p = 0.001, CI, - 4.74 to -1.52) in the successful NIV group although the duration of hospital stay was not different between the two groups (*Table 4*).

Table 4: Duration of NIV, ICU stay and hospital stay in the groups

Duration (days)	NIV Success (n = 26)	NIV failure (n = 15)	P value
NIV	2.7 ± 0.9	1.6 ± 0.7	< 0.001
ICU stay	4.6 ± 1.4	7.7 ± 3.6	0.001
Hospital stay	15 ± 7.7	14.7 ± 6.7	0.92

Discussion

The present study was aimed at analysing the clinical outcome and the factors associated with success and failure of use of NIV in patients with ARF. Success rate (63.4%) of NIV in acute respiratory failure in this study is similar to that of Antonelli *et al*[9] (62%) and Rocker GM *et al*[10] where they found 62% and 66% success respectively demonstrating that the use of NIV can benefit patients in acute respiratory failure.

Antonelli *et al* investigated the application of NIV as a first-line intervention in patients with early acute respiratory distress syndrome (ARDS) and concluded that NIV applied as first-line intervention in ARDS avoided intubation in 54% of treated patients and that a SAPS II >34 and the inability to improve PaO_2/FiO_2 after 1 hour of NIV were predictors of failure.[11] In the present study, patients who succeeded in NIV trial had a significant increase in PaO_2 at 1 hour and it continued to be significantly higher even at 6 hours of the trial. The patients in NIV failed group seemed to have a higher mean $PaCO_2$ and lower pH than in the NIV success group. The difference in the numbers between the groups was clinically significant although it did not attain statistical significance. The respiratory rate decreased in both groups with NIV but did not predict the course of NIV.

Although those patients who improved with NIV required it for a longer time, the duration of their ICU stay was shorter. The reasons for failure of NIV that necessitated endotracheal intubation were mainly an inability to correct hypoxaemia and hypercarbia, and occasionally inability to clear secretions, haemodynamic instability and deterioration of consciousness.

A recent paper by Chettino S *et al* reported that NIV failure in acute hypoxaemic respiratory failure was associated higher mortality.[12] Although 63% success rate was seen in the present study with NIV in patients with acute hypoxaemic respiratory failure, out of the 15 patients who failed NIV, 14 died (93.3%). Such a high mortality rate may have been due to factors such as haemodynamic instability due to sepsis, underlying malignancy or even delay in intubation due to NIV.

It may be argued that those patients with haemodynamic instability and underlying malignancy (for which major surgery was done) may have died even if they had received invasive ventilation as a primary treatment. However, the possibility of increased mortality due to delay in

endotracheal intubation and mechanical ventilation cannot be ignored.

Keenan SP *et al* in their systematic review found out that the addition of NIV to standard care in the setting of acute hypoxaemic respiratory failure reduced the rate of endotracheal intubation (absolute risk reduction 23%, 95% confidence interval 10-35%), ICU length of stay (absolute reduction 2 days, 95% confidence interval 1-3 days), and ICU mortality (absolute risk reduction 17%, 95% confidence interval 8-26%).[13]

The limitation of the present study was that it was an observational study and the sample size was comparatively small. Even then, this study seems to bring to light important clinical findings.

Conclusion

A trial of NIV may be offered to eligible patients with acute respiratory failure. NIV when successful is associated with shorter ICU stay and its failure, with high mortality. The effectiveness of NIV in improving oxygenation in the initial hours could be used to predict whether the patients with acute respiratory failure may be successfully treated with NIV and also to avoid unnecessary delay in intubating patients who deteriorate on NIV. It is also possible that invasive ventilation may be more appropriate for patients with primary pulmonary cause for respiratory failure. A larger study is required to confirm these findings.

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