Noninvasive ventilation in acute hypoxic respiratory failure in medical intensive care unit: A study in rural medical college

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ABSTRACT

Introduction: Noninvasive ventilation (NIV) has emerged as an important tool for the management of acute hypoxic respiratory failure (AHRF) and has been the area of research in the last two decades. In this study, we have tried to find out the outcome of NIV in patients with AHRF.

Materials and Methods: In this prospective, observational study, all the patients of AHRF requiring NIV were enrolled, and heart rate (HR), respiratory rate (RR), arterial blood gas parameters, and NIV settings at baseline, 1 h, and 4 h were collected. The patients were classified as AHRF with acute respiratory distress syndrome (ARDS) and AHRF without ARDS, which were further classified according to the outcome.

Results: Among 200 patients admitted in medical intensive care unit (ICU), 50 patients (27 with ARDS and 23 without ARDS) were put on NIV. There was a significant improvement in HR, RR, PaO₂, and inspiratory positive airway pressure after 1 and 4 h and significant improvement at 4 h in expiratory positive airway pressure in all the groups on NIV. Length of ICU stay and hospital stay was less in the nonintubated group. Mortality rate was 25.92% in the intubated group, while it was nil in the nonintubated group.

Conclusion: NIV found to reduce the endotracheal intubation and mortality, by improving the outcome of the patient.

Key Words: Acute hypoxic respiratory failure, acute lung injury, acute respiratory distress syndrome, noninvasive ventilation

IMPLICATIONS OF CLINICAL PRACTICE

- Noninvasive ventilation is the modality of treatment in the selected patients of acute hypoxic respiratory failure
- Depending on the response of the patients, monitoring, and various baseline parameters, further management needs to be decided so that intubation would not be delayed
- The early introduction of noninvasive ventilation can reduce the rate of intubation and subsequent complications and infections associated with intubation

INTRODUCTION

Noninvasive ventilation (NIV) provides positive pressure airway support through a face or nasal mask without the use of an endotracheal tube, being used as the first-line management of acute hypoxic respiratory failures (AHRF). The advantages of NIV include no requirement for endotracheal intubation (ETI), which lowers the risk of ventilator-associated pneumonia, lowers the
intensive care unit (ICU) length of stay, and decreases hospitalization costs.\cite{1}

It is initiated as the first-line ventilatory support in 20%–30% of AHRF patients.\cite{2,3} NIV has even been used as main treatment in patients having clinical criteria for acute respiratory distress syndrome (ARDS) with a success rate of >50%, especially in patients with prompt improvement of oxygenation.\cite{4}

The use of NIV in AHRF has been an area of research over the last two decades with several studies published.\cite{2–10} Controversy exists as to whether NIV is appropriate in all forms of AHRF. The largest proven benefit is confined to patients with severe exacerbations of chronic obstructive pulmonary disease (COPD) and asthma and with hypercarbia.\cite{5} While the results from patients with AHRF are conflicting, the outcome of interest may be the avoidance of ETI and its potential complications. Two recent meta-analyses did not find any strong evidence to support the role of NIV in AHRF and ARDS.\cite{11,12}

However, few randomized controlled trials support NIV in AHRF due to pneumonia in immunocompromised hosts and after lung resection surgery as it had reduced the need for intubation and even mortality.\cite{13–15} In some cases of cardiogenic pulmonary edema leading to AHRF, the use of NIV has shown to reduce mortality in the meta-analysis, but a recent large trial failed to demonstrate any survival advantage.\cite{16,17}

As a matter of concern, some patients may initially benefit from NIV (for hours to a few days) but may deteriorate and require intubation. Failure to identify the patients who are likely to fail NIV can cause an inappropriate delay of intubation and can lead to clinical deterioration in these patients with increased morbidity and mortality.\cite{18,19}

This subject of NIV in AHRF has been widely researched, with data published from the developed world but not much data from India.\cite{14,13,19,20} Hence, the study was undertaken to ascertain the beneficial role and outcome of NIV in AHRF in the medical ICU (MICU) at a rural teaching medical college.

**MATERIALS AND METHODS**

This prospective, observational study was carried out at a teaching hospital of rural medical college from September 2016 to August 2017, after ethical clearance taken from the Institute Ethical Committee (reference no.: IEC-2016/1487). All the consecutive patients of AHRF admitted in the MICU requiring NIV were enrolled in the study after taking proper consent.

The demographic details of patients such as age, sex, body mass index (BMI), etiology of AHRF, and presence and absence of associated comorbid illnesses were recorded. The disease severity was calculated using the Acute Physiology and Chronic Health Evaluation II (APACHE II) scores. We collected the data for heart rate (HR), respiratory rate (RR), and arterial blood gases (ABGs – pH, PaO₂, PaCO₂) at baseline, 1 h, and 4 h.

Patients were included in the study on the basis of clinical signs and symptoms of acute respiratory distress, RR >30 breaths/min, use of accessory muscles of respiration, paradoxical breathing, and ABG analysis with ratio of PaO₂ to fraction of inspired oxygen (PaO₂/FiO₂) <300 mmHg or PaO₂ <60 mmHg on oxygen through an air mask. Patients were excluded who need the following:

- Immediate ETI
- Multiple organ dysfunction
- Inability to protect airway (excess secretions, drowsy, or comatose patient)
- Cardiogenic pulmonary edema
- Abnormalities that preclude proper fit of the interface (agitated or uncooperative patient, facial trauma or burns, facial surgery, or facial anatomical abnormality)
- The patient already on mechanical ventilation
- The patient not giving the consent.

**Definition of acute hypoxic respiratory failure**

AHRF was defined as recent dyspnea with an RR >25 breaths/min and/or sternocleidomastoid muscle activation with pulmonary infiltrates on chest X-ray and a PaCO₂ ≤45 mmHg.\cite{21}

**Criteria for endotracheal intubation**

Loss of consciousness or psychomotor agitation hindering nursing care and requiring sedation; persistent hypotension (defined by systolic arterial blood pressure <90 mmHg or mean arterial blood pressure <65 mmHg) despite fluid resuscitation, or need for vasopressors; or two of the following criteria: frank worsening of respiratory distress under NIV, RR >40 breaths per min, dependence to NIV for >12 h, or pH <7.35. NIV failure was defined by the need for ETI.\cite{21}

**Methods**

NIV was administered with the use of a portable noninvasive ventilator by Sullivan VPAP II ST-Australia, after explaining its detailed procedure to the patient for better compliance. NIV was delivered to patients in bed with propped up position. Oxygen supplementation was provided through a port in the mask, to keep arterial oxygen saturation >90%. Pressure-support ventilation was started using a pressure-support level of 8 cmH₂O, a positive end-expiratory pressure level of 5 cmH₂O, an inspiratory trigger of 3 L/min, and a maximal inspiratory time of 1 s. The inspiratory and expiratory
pressure (inspiratory positive airway pressure [IPAP] and expiratory positive airway pressure [EPAP]) was titrated in increments of 2 cmH$_2$O, based on continuous pulse oximetry to achieve arterial oxygen saturation of minimum 90%, improvement in patient’s dyspnea, and decreased RR.

ICU nurses were directed to check the presence of air leaks, and accordingly, the patient was constantly encouraged and reassured. The NIV was applied for as long as possible in the initial 24 h with intermittent periods off for eating and expectoration of secretions. Oxygen was delivered through an air mask during the off period.

Weaning from NIV was done by reducing the duration of NIV to 5–6 h/day if the RR remained <24 breaths/min and PaO$_2$ >60 mmHg without any ventilator support. The primary outcomes of the patients were need of intubation, duration of hospital stay, and length of ICU stay, and the secondary outcome was overall mortality.

**Statistical analysis**

The data were collected and stored in an electronic spreadsheet (Microsoft Excel 2016, Redmond, Washington, USA). Statistical analysis was done using descriptive and inferential statistics using mean ± standard deviation, Chi-square test, Student’s paired $t$-test, and Student’s unpaired $t$-test, and software used in the analysis were SPSS 22.0 version (Statistical Package for the Social Sciences, International Business Machines (IBM) Corporation, USA) and GraphPad Prism 6.0 version (GraphPad Software Inc., California Corporation), and $P < 0.05$ was considered as level of significance.

**OBSERVATIONS AND RESULTS**

During the study period, among 200 patients of AHRF admitted in MICU, 116 patients were put on invasive ventilation and 34 patients were on oxygen therapy alone, while 50 patients were put on NIV. All 50 patients on NIV were divided into two groups according to the etiology (AHRF with ARDS and AHRF without ARDS) and further subdivided according to the outcome as intubated (NIV failure) and nonintubated group on NIV as shown in flowchart [Figure 1].

Baseline characteristics of the patients receiving NIV are shown in Table 1. The mean age of the patients was 52.96 ± 16.72 years in ARDS, while it was 50.65 ± 18.81 years in non-ARDS group. The mean HR was 124.48 ± 14.42 beats/min and 122.26 ± 15.48 beats/min in ARDS and non-ARDS group, respectively. The mean PaO$_2$/FiO$_2$ ratio was 143.33 ± 94.40 in ARDS and 196.82 ± 106.64 in non-ARDS group ($P = 0.06$, not significant). All other parameters are shown in Table 2.

Table 3 shows HR, RR, pH, PCO$_2$, PO$_2$, IPAP, and EPAP at 0 h, 1 h, and 4 h in ARDS group receiving NIV. Out of 27 patients, 11 (40.74%) were intubated in this group. RR was 37.54 ± 3.50, 35.09 ± 2.87, and 31.00 ± 4.12 and 37.37 ± 4.24, 35.62 ± 4.08, and 31.75 ± 3.15 breaths/min in intubated group ($P = 0.001$, $P = 0.0001$) and nonintubated group ($P = 0.025$, $P = 0.0001$), respectively, at 0 h, 1 h, and 4 h. PCO$_2$ was 32.18 ± 6.52, 31.63 ± 6.28, and 31.72 ± 8.71 and 33.50 ± 7.50, 33.06 ± 7.07, and 33.81 ± 7.11 mmHg in intubated group ($P = 0.53$, $P = 0.82$) and nonintubated group ($P = 0.53$, $P = 0.80$), respectively, at 0 h, 1 h, and 4 h. PO$_2$ was 57.63 ± 9.00, 73.90 ± 13.81, and 86.18 ± 33.08 and 81.56 ± 37.61, 117.02 ± 35.31 mmHg in intubated group ($P = 0.001$, $P = 0.021$, significant) and nonintubated group ($P = 0.001$, $P = 0.0001$, significant), respectively, at 0 h, 1 h, and 4 h. IPAP was 10 ± 2.19, 14.54 ± 1.57, and 16 ± 0.89 and 9.37 ± 4.08, 14.25 ± 2.04, and 15.62 ± 1.31 cmH$_2$O in intubated group ($P = 0.001$, $P = 0.0001$, significant) and nonintubated group ($P = 0.0001$, $P = 0.0001$, significant), respectively, at 0 h, 1 h, and 4 h.
4 h. EPAP was 4.72 ± 0.78, 5.45 ± 1.29, and 6.36 ± 0.80 and 4.81 ± 0.75, 5.37 ± 0.95, and 6.25 ± 1.00 cmH\(_2\)O in intubated group (\(P = 0.070\), not significant, \(P = 0.0001\), significant) and nonintubated group (\(P = 0.132\), not significant, \(P = 0.002\), significant), respectively, at 0 h, 1 h, and 4 h.

In non-ARDS group receiving NIV, 8 patients (34.78%) were intubated out of 23. Various parameters at 0 h, 1 h, and 4 h are shown in Table 4. \(\text{PCO}_2\) was 35.62 ± 2.97, 33.87 ± 4.15, and 34.37 ± 4.37 and 33 ± 7.54, 32.45 ± 4.99, and 32.93 ± 5.56 mmHg in intubated group (\(P = 0.13\), \(P = 0.31\)) and nonintubated group (\(P = 0.60\), \(P = 0.97\)), respectively,

### Table 2: Comparison of baseline characteristics of patients receiving noninvasive ventilation, according to various etiology

|                        | AHRF with ARDS (n = 27) | AHRF without ARDS (n = 23) | Total (n = 50) | \(P\) |
|------------------------|-------------------------|-----------------------------|----------------|-----|
| Age (years)            | 52.96 ± 16.72           | 50.65 ± 18.81               | 51.90 ± 17.56  | 0.64 (NS) |
| APACHE II score        | 13.40 ± 6.36            | 12.04 ± 5.49                | 12.78 ± 5.96   | 0.42 (NS) |
| HR (beats/min)         | 124.46 ± 14.42          | 122.26 ± 15.48              | 123.46 ± 14.80 | 0.60 (NS) |
| RR (breaths/min)       | 37.44 ± 3.88            | 37.08 ± 4.06                | 37.28 ± 3.93   | 0.75 (NS) |
| pH                     | 7.34 ± 0.04             | 7.36 ± 0.03                 | 7.35 ± 0.03    | 0.078 (NS) |
| \(\text{PaO}_2/\text{FiO}_2\) | 143.33 ± 94.40         | 196.82 ± 106.64             | 167.94 ± 102.76 | 0.06 (NS) |
| \(\text{PaCO}_2\) (mmHg) | 32.96 ± 7.02            | 33.91 ± 6.37                | 34.00 ± 6.68   | 0.62 (NS) |

AHRF: Acute hypoxic respiratory failure, ARDS: Acute respiratory distress syndrome, APACHE: Acute Physiology and Chronic Health Evaluation, HR: Heart rate, RR: Respiratory rate, NS: Not significant, \(\text{PaO}_2/\text{FiO}_2\): Arterial oxygen pressure/fraction of inspired oxygen, \(\text{PaCO}_2\): Arterial carbon dioxide pressure

### Table 3: Serial clinical and arterial blood gas parameters in acute respiratory distress syndrome group receiving noninvasive ventilation

|                        | Intubated (n = 11) | Nonintubated (n = 16) | \(P\) |
|------------------------|-------------------|-----------------------|-----|
| 0 h                    |                   |                       |     |
| HR (beats/min)         | 125.63 ± 14.90    | 119.36 ± 13.19;       | 0.01 |
| RR (breaths/min)       | 37.54 ± 3.50      | 35.09 ± 2.87;         | 0.01 |
| pH                     | 7.34 ± 0.05       | 7.40 ± 0.19;          | 0.05 |
| \(\text{PCO}_2\) (mmHg) | 32.18 ± 6.52      | 31.63 ± 6.28;         | 0.53 |
| \(\text{PO}_2\) (mmHg) | 57.63 ± 9.00      | 73.90 ± 13.81;        | 0.53 |
| IPAP (cmH\(_2\)O)     | 10.21 ± 2.19      | 14.54 ± 1.57;         | 0.001|
| EPAP (cmH\(_2\)O)     | 4.72 ± 0.78       | 5.45 ± 1.29;          | 0.001|
| \(\text{PaO}_2/\text{FiO}_2\) | 101 ± 9.45       | 108.27 ± 14.76;       | 0.001|

HR: Heart rate, RR: Respiratory rate, \(\text{PaO}_2/\text{FiO}_2\): Arterial oxygen pressure/fraction of inspired oxygen, \(\text{PaCO}_2\): Arterial carbon dioxide pressure, \(\text{PO}_2\): Arterial oxygen pressure, IPAP: Inspiratory pressure, EPAP: Expiratory pressure, AHRF: Acute hypoxic respiratory failure, ARDS: Acute respiratory distress syndrome

### Table 4: Serial clinical and arterial blood gas parameters in acute hypoxic respiratory failure without acute respiratory distress syndrome group receiving noninvasive ventilation

|                        | Intubated (n = 8) | Nonintubated (n = 15) | \(P\) |
|------------------------|------------------|-----------------------|-----|
| 0 h                    |                   |                       |     |
| HR (beats/min)         | 117.87 ± 15.04   | 109.76 ± 10.81;       | 0.009|
| RR (breaths/min)       | 38.87 ± 5.22     | 33.50 ± 4.37;         | 0.003|
| pH                     | 7.36 ± 0.03      | 7.38 ± 0.03;          | 0.08 |
| \(\text{PCO}_2\) (mmHg) | 36.62 ± 2.97     | 33.87 ± 4.15;         | 0.43 |
| \(\text{PO}_2\) (mmHg) | 61.37 ± 9.60     | 72.67 ± 16.19;        | 0.048|
| IPAP (cmH\(_2\)O)     | 7.25 ± 2.60      | 14.50 ± 1.41;         | 0.0001|
| EPAP (cmH\(_2\)O)     | 5 ± 0.75         | 5 ± 1.06;              | 0.001|
| \(\text{PaO}_2/\text{FiO}_2\) | 147.25 ± 9.45    | 120.4 ± 13.84;        | 0.013|

HR: Heart rate, RR: Respiratory rate, \(\text{PaO}_2/\text{FiO}_2\): Arterial oxygen pressure/fraction of inspired oxygen, \(\text{PaCO}_2\): Arterial carbon dioxide pressure, \(\text{PO}_2\): Arterial oxygen pressure, IPAP: Inspiratory pressure, EPAP: Expiratory pressure, AHRF: Acute hypoxic respiratory failure, ARDS: Acute respiratory distress syndrome
at 0 h, 1 h, and 4 h. PO$_2$ was 61.37 ± 9.60, 72.67 ± 16.19, and 75.50 ± 10.47 and 88.66 ± 31.78, 109.21 ± 30.17, and 126.93 ± 33.29 mmHg in intubated group (P = 0.048, P = 0.012) and nonintubated group (P = 0.039, P = 0.001), respectively, at 0 h, 1 h, and 4 h. IPAP was 7.25 ± 2.60, 14.50 ± 1.41, and 16 ± 1.06 and 8.13 ± 2.32, 14 ± 1.30, and 15.73 ± 1.03 cmH$_2$O in intubated group (P = 0.0001, P = 0.0001) and nonintubated group (P = 0.0001, P = 0.0001), respectively, at 0 h, 1 h, and 4 h. EPAP was 5.7 ± 0.75, 5 ± 1.06, and 7.25 ± 1.03 cmH$_2$O in intubated group and 4.80 ± 0.86, 4.93 ± 1.27, and 6.40 ± 0.82 in nonintubated group at 0 h, 1 h, and 4 h. Mean PaO$_2$/FiO$_2$ ratio in the intubated group was 120.47 ± 54.56 while in nonintubated was 186.77 ± 78.94 (P = 0.002). Mean PaCO$_2$ in intubated and nonintubated group was 33.63 ± 5.48 mmHg, respectively (P = 0.85). Seven male patients (36.84%) and 16 male patients (51.61%) were in intubated and nonintubated group, respectively (χ$^2$ = 1.04, P = 0.30). Eleven patients out of 19 (57.89%) were intubated and 16 patients out of 31 (51.61%) were nonintubated in ARDS etiology (χ$^2$ = 0.18, P = 0.66) [Table 5].

Table 6 shows a comparison of outcome parameters in intubated and nonintubated patients having AHRF with ARDS and AHRF without ARDS. The mean duration of ICU stay was 11 ± 7.50 and 9.06 ± 7.51 days in intubated and nonintubated patients, respectively. The mean duration of hospital stay was 12.81 ± 7.44 and 11.62 ± 6.46 days in intubated and nonintubated patients, respectively. Mortality rate was 25.92% in the intubated group, while it was nil in the nonintubated group. In Table 7, we have shown the outcome of all patients receiving NIV.

### DISCUSSION

In the present study, we found the beneficial role of NIV in AHRF in the MICU as an improvement in gas exchange and so necessity of intubation. In AHRF with ARDS group, only 40% were intubated, and in AHRF without ARDS, only 34% were intubated.

In this study, the factors that affected NIV were severity of underlying illness and APACHE score. Comorbid conditions such as diabetes, hypertension, and ischemic heart disease did not affect likelihood of failure of NIV.

On linear regression analysis, there was statistically significant outcome in EPAP and IPAP in both the groups on NIV on somewhat longer duration, i.e., at 4 h, it had the largest effect on outcome (i.e., to prevent intubation). We were able to use NIV in 25% of admissions with AHRF, which reflects the fact that only few patients with AHRF receive NIV.

The baseline APACHE II score was not associated with NIV failure in our study as we excluded patients with multiple organ dysfunction syndrome. In our study, in ARDS (both intubated and nonintubated) groups, PO$_2$, HR, and RR showed significant improvement at 1 h
and 4 h as compared to 0 h with improvement in ABG parameter as well, while the same effect was noted in non-ARDS group. Similar observation was noted in other studies as well.[21,22]

Numerous studies have investigated the role of NIV in AHRF and showing as effective as conventional ventilation in correcting gas exchange. They also showed that the presence of multiple organ dysfunctions, shock, and severity of illness, as determined by ICU severity score, has predicted failure of NIV.[23‑26]

NIV failure occurs in those patients with AHRF which are mainly due to ARDS, and it was reported as almost 51% in a large multicenter study, in contrast to 10% in cardiogenic pulmonary edema.[4,20]

In the study conducted by Singh et al., they found significant improvement in HR and RR at 1 h in the hypoxic group who were on NIV, similar to our study.[27] This suggests that NIV has benefit in AHRF patients.

We observed that if patients were put on NIV, their duration of ICU stay and requirement of intubation also became less. The mean duration of ICU stay was 11 ± 7.50 and 9.06 ± 7.51 days in intubated and nonintubated group, respectively, in ARDS group. In non-ARDS group, mean duration of ICU stay was 11.62 ± 9.94 and 5.93 ± 3.67 days in intubated and nonintubated group, respectively. Agarwal et al. also observed the same results.[21]

In our study, the outcome in all the patients receiving NIV was that among 50 patients, 19 patients were intubated of which seven patients survived, whereas all patients survived in nonintubated group. The success rate found in the present study was 76%. Our result was comparable to other authors.[20,22,28]

Although there is a strong pathophysiological basis for the role of NIV in AHRF, the evidence on the role of NIV in AHRF does not support its routine use. The syndrome of ARDS represents a group of heterogeneous etiologies of variable severities, and hence, the benefits of NIV in this syndrome have been variable. In fact, for similar degrees of hypoxemia, the outcome of NIV depends on the underlying pathophysiologic mechanisms responsible for AHRF. Hence, NIV should be initiated in selected patients of AHRF patients.

**Limitation**

The observational design of our study had few limitations. Our sample size was small so cannot be generalized in all ARDS groups. We had not taken into consideration of other causes of AHRF such as pneumonia, COPD, bronchial asthma, and interstitial lung disease as sometimes there may be problems in differentiating between them and might be classified as forms of ARDS. We also did not consider BMI as the use of NIV in patients of higher BMI (having a component of pulmonary edema, [whether noncardiogenic from ARDS or cardiogenic, renal failure, and iatrogenic fluid administration], COPD, or interstitial lung disease); all are very different in their requirements for ventilation and oxygenation both with NIV and mechanical ventilation. We did not assess whether mortality in our patients was because of delay in implementation of ETI. The last limitation was, in this study, both IPAP and EPAP were titrated in increments of 2 cmH₂O; however, to optimize management of hypoxia (especially severe hypoxia), the EPAP should be the focus for titration rather than IPAP separately. This may have changed the outcome on some patients, especially the obese ones who require higher EPAPs to help keep their upper airway open.

**CONCLUSION**

NIV is good modality in AHRF patients as it is easy to use and having less complication rate as compared to invasive ventilation. Depending on the clinical scenario and association of risk factors, comorbidity, and disciplined monitoring in patients with AHRF, NIV should be started meticulously after thorough scrutiny and screening of all these factors.

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**Conflicts of interest**

There are no conflicts of interest.

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