ORIGINAL RESEARCH

Arterial blood gas as a predictor of successful non-invasive ventilation outcome in COPD patients with type 2 respiratory failure

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Received: 12March, 2023 Accepted: 18April, 2023

ABSTRACT

Introduction: The application of NIV in the management of patients with acute respiratory failure is not associated with a 100% success rate. In many patients, application of NIV is clearly insufficient as it does not obtain adequate ventilation and eventually endotracheal intubation and invasive mechanical ventilation is required for the management of respiratory failure. Failure to identify the patients who are likely to fail NIV can cause inappropriate delay in intubation; this can lead to clinical deterioration and increased morbidity and mortality. The failure rates of NIV can range from 5% to 50% in different studies depending on the etiology and severity of respiratory failure.

Objective: To evaluate initial Arterial blood gas as a predictor of successful NIV outcome in patients with type 2 respiratory failure in a tertiary care hospital in south Kerala.

Methods: Based on longitudinal observational study, 80 adult patients diagnosed with Type 2 Respiratory failure were admitted to hospital requiring NIV. NIV-PSV (pressure support mode) were used in all patients. All patients were given oxygen and titrated during ventilation to maintain oxygen saturation between 88%-92%. Serial ABG were studied and if clinical or ABG value worsening were noted, they were proceeded for invasive ventilation. Weaning was initiated on clinical improvement and corroborative ABG values.

Results: Out of the 80 patients admitted with type 2 respiratory failure, success rate with NIV was found to be 77.5% with 62 patients discharged successfully. Failure rate was 22.5% (18 patients). Of the failed 18 patients, 17 were mechanically ventilated and 1 expired on NIV as no consent for endotracheal intubation were given by the bystanders. 6 other patients who were mechanically ventilated also eventually succumbed. Patient with initial pH between 7.30-7.35 had shown better outcome (71%) as compared to pH between 7.25-7.30 which was statistically significant, p<0.001(Chi Square test) and with initial $PaCo_2$ between 45-85 mmHg had shown better outcome (67.7%+29%) as compared to patient with initial $PaCo_2$>85 and it is statistically significant, p<0.001(Chi Square test).

Conclusion: Present study suggests that NIV is highly effective in treating patients with type 2 respiratory failure with pH 7.25-7.35. This study also shows that patients with high initial PaCo2 and low pH have lower chance of success with NIV. Study indicates that a trial of NIV is effective in improving gas exchange, reducing intubation in patients with type 2 respiratory failure, suggesting that NIV is a safe and effective means of ventilator support for patients with type 2 respiratory failure. The study provides strong evidence for the use of NIV as a first line intervention in patients with type 2 respiratory failure, irrespective of the cause of respiratory failure.

Key words:ABG-Arterial Blood Gas; BPAP-Bi-level Positive Airway Pressure COPD-Chronic Obstructive Pulmonary Disease; pH-Potential of Hydrogen; NIV-Non-Invasive Ventilation; ETI- Endotracheal intubation

Introduction

NIV refers to the provision of ventilator support through the patient's upper airway using a mask or similar device[1]. NIV has revolutionized the management of acute respiratory failure, and has been applied in diverse forms of acute respiratory failure. NIV has been a standard treatment approach to patients with type 2 respiratory failure and is recommended as the initial intervention for most patients with Type 2 respiratory failure unless specific contraindications exist.

The frequency of type 2 respiratory failure in patients with acute exacerbation of COPD varies from 16-35% with overall mortality of 35-43%. Ventilatory support via endotracheal intubation (ETI) is the standard mode of therapy, for such patients. However, ETI is associated with several complications including nosocomial pneumonia, injury to upper airways causing ulceration, hemorrhage and long-term complication like tracheal stenosis. Moreover, patients with COPD are prone to ventilator dependence and may have repeated weaning failures leading to requirement of tracheostomy. It is obvious that avoiding ETI in patients with acute exacerbation of COPD is the key to improving their in-hospital outcomes. To this end, NIV has been claimed to be a safe and effective alternative in patients with acute exacerbation of COPD.[2-4] Potential advantages of using NIV include avoidance of tracheal intubation and its associated morbidity and mortality. On NIV, patients are able to eat, drink, cough and expectorate and take oral medications by taking break from NIV treatment.

The application of NIV in the management of patients with acute respiratory failure is not associated with a 100% success rate. In many patients' application of NIV is clearly insufficient as it does not obtain adequate ventilation and eventually endotracheal intubation and invasive mechanical ventilation is required for the management of respiratory failure. Also, some patients will initially benefit from NIV (for hours to few days) but will then deteriorate and require intubation. The failure rates of NIV can range from 5% to 50% in different studies depending on the etiology and severity of respiratory failure (Plant *et al* 2001[5], Nava and Ceriana 2004[6]; Confalonieri *et al* 2005[7]).

Failure to identify the patients who are likely to fail NIV can cause inappropriate delay in intubation; this can lead to clinical deterioration and increased morbidity and mortality. Thus, it becomes important to ascertain the factors associated with NIV failure so that we can identify the high-risk subset of patients who are likely to fail a trial of NIV.

However, there is still a paucity of literature from India on NIV despite the fact this modality of treatment can assume significant relevance in resource constrained setting[8].

In this study, we wanted to assess ABG as a predictor tool as for successful NIV outcome in patients with type 2 respiratory failure in a tertiary care hospital in south Kerala.

Materials and Methods

After getting permission from the Institutional Ethics Committee (No. PIMSRC/E1/388A/43/2019), a longitudinal observational study was conducted on 80 COPD patients with Type 2 Respiratory failure admitted to the department of Respiratory Medicine, for a period of 2 years, from November 2019 to October 2021.

All patients above 18 years of age, with diagnosed type 2 respiratory failure (PH<7.35 and $PaCO_2$>45mmHg, PaO_2<60mmHg, SpO_2<92% with 4-6 l/min oxygen by mask), who were conscious and cooperative, and on whom airway was able to be maintained, were included in this study after getting a written informed consent.

Whereas, those who were not conscious nor cooperative, those whom airway was not able to be maintained and those who suffered from facial injuries, who had hemodynamic instability with life threatening hypoxia were excluded from this study.

NIV (pressure support mode) will be used in all patients. Ventilator is equipped with adjustable pressure limits and patient is ventilated as per the predefined inspiratory and expiratory airway pressure settings with each inspiration being triggered by patient's spontaneous breath. The interface used during the study was a well-fitting Oro-nasal mask. After explaining the details of the process of the NIPPV institution, patient was propped up to 30-degree angle. NIPPV was initiated by the investigators in all the cases. Patient were usually initiated on a pressure support (PS) and end expiratory positive airway pressure (EPAP) of8 cm H_2O and 5 cm H_2O. Subsequent adjustments were carried out according to the need of the patient and the results of blood gas analysis. All patients were given oxygen and titrated during ventilation to maintain oxygen saturation between 88%-92%.

Each patient was encouraged to use the NIV continuously. NIV was discontinued for eating and drinking. After starting treatment each patient was monitored closely. Patient's discomfort and intolerance to mask was looked for. Clinical status such as use of accessory muscles of respiration, increase or decrease of dyspnea, appearance or disappearance of cyanosis, heart rate, respiratory rate, blood pressure was monitored. Level of consciousness were also closely monitored. Continuous arterial oxygen saturation was monitored using pulse oximeter. ABG analysis done at 1–2-hour, 4-6 hour and any other time if patient's condition required so, any deterioration of pH (pH<7.25) and increase PaCO2, worsening of mental

status (Glasgow coma scale <8), hemodynamic instability, intolerance to NIV, and such patients shall proceed to invasive ventilation.

All the patients received pharmacological treatment including bronchodilators, steroids, antibiotics, DVT prophylaxis, and nebulization, decided on case-to-case basis and as per the standard guidelines.

Once the patient improved clinically and corroborated by improvements in ABG, weaning was initiated. During the weaning phase, the pressure support was decreased in gradations of 2-3 cm H_2O till the inspiratory positive airway pressure was 8 cm H_2O. The application was switched over to intermittent use. Weaning failure was defined as inability to wean the patient off NIV, due to clinical features such as respiratory distress (tachypnea, tachycardia, and increased work of breathing) or laboratory evidence of worsening or persistent respiratory distress.

Data was entered in Microsoft Excel and analyzed. Categorical data was presented as frequency and percentage and continuous data such as age as descriptive statistics. Association between NIV outcome and demographic and clinical characteristics were done using Chi-square/ Fisher's exact tests. A p value of <0.05 was considered as statistically significant.

Results

Among the 80 COPD patients who met the inclusion criteria admitted with type 2 respiratory failure during the period of November 2019 to October 2021, these were our findings:

Success rate with NIV was 77.5% with 62 patients discharged successfully. Failure rate was 22.5% (18 patients). Of the failed 18 patients, 17 were mechanically ventilated and 1 expired on NIV as no recorded action for endotracheal intubation were taken and conscious decision not to escalate therapy and the decision was taken subsequent to recruitment to the trial after discussing with prognosis and further treatment option with the relatives. 6 other patients who were mechanically ventilated also eventually succumbed.

NIV outcome

Outcome of NIV in the study population is depicted in table: 1, Fig.1.

Table 1: Outcome of NIV use in the study group

Subject on NIV	Frequency(n)	Percentage (%)
Success	62	77.5
Failure	18	22.5
Total	**80**	**100**

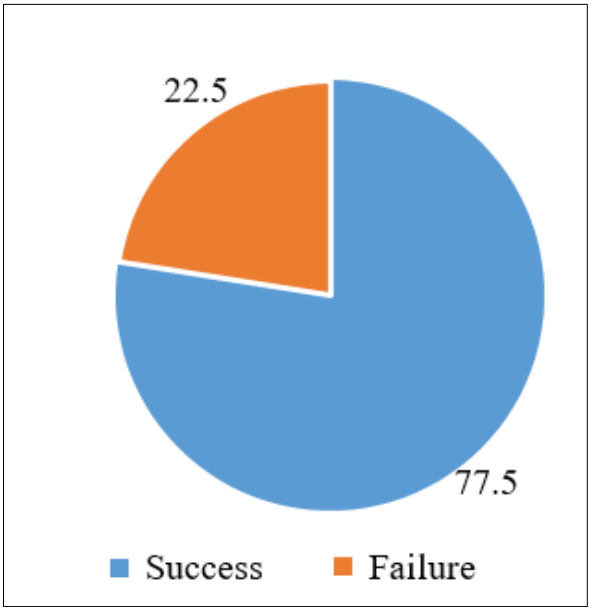

Fig1: Outcome of NIV use in the study group

Patients with pH between 7.30-7.35 had shown better outcome (71%) as compared to pH between 7.25-7.30 which was statistically significant, p<0.001(Chi Square test). (table 2).

Table 2: Effect of initial pH on outcome

pH range	Outcome Success	Outcome Failure	Total
7.35-7.30	44(71.0%)	2(11.1%)	46
7.30-7.25	18(29.0%)	16(88.9%)	34
Total	62	18	80

Table 3: Effect of initial $PaCo_2$ on NIV outcome

$PaCo_2$ range (mm Hg)	Outcome Success	Outcome Failure	Total
45-65	18(29.0)	1(5.6%)	19
65-85	42(67.7%)	10(55.6%)	52
85-105	2(3.2%)	7(38.9%)	9
Total	62	18	80

No association was noted between initial Pao_2 and NIV outcome, p <0.334(Chi Square test). (table 4).

Table 4: Effect of Pao_2on NIV outcome

Pao_2 range (mm Hg)	Outcome Success	Outcome Failure	Total
40-50	6(9.7%)	4(22.2%)	10
50-60	53(85.5%)	13(72.2%)	66
Above 60	3(4.8%)	1(5.6%)	4
Total	**62**	**18**	**80**

Discussion

The use of non-invasive ventilation has markedly increased for the past two decades and non-invasive ventilation has now become an integral tool in the management of both acute and chronic respiratory failure in both at home setting and in the critical care unit. Non-invasive ventilation has been used as a replacement for invasive ventilation as its flexibility also allows it to be a valuable complement in patient management. The role of NIV has been studied and was found to be more useful as an effective therapeutic modality along with other standard treatment.

Non-invasive ventilation is a cost effective, readily available technique and can be used readily outside the intensive care settings. The advantages of non-invasive ventilation include patient comfort, preservation of airway defenses like cough, ability to speak and eat. The complications of endotracheal intubation such as nosocomial pneumonias, injury to airways, aspiration, and post intubation laryngeal stenosis could be avoided.

Early initiation of NIV is recommended so patients have time to adapt and respiratory crises can be averted. On the other hand, NIV begun too early might be unhelpful and wasteful of resources if treated patients would have done well without any ventilatory assistance. For this reason, selection guidelines suggest first establishing the need for ventilatory assistance according to clinical and blood gas criteria and exclusion of patients in whom NIPPV is contraindicated or likely to fail[9].

Confalonieri *et al*. examined predictive factors related to NIV failure in a large multicenter study which included 1033 patients with severe AECOPD. In their study, pH values, respiratory rate, GCS, and APACHE II severity score recorded at t0 and t1 were found to be independent predictive variables for NIV failure. These variables were then used to build a prognostic model for NIV failure, which proved to have high accuracy, especially at t1 when assessed on an independent sample of patients. Specifically, a pH < 7.25 at t1 was an important predictive indicator of NIV failure[7].

In general, factors predicting success/failure with NIV in type 2 respiratory failure include pH at admission, pH after one hour of NIV trial and severity of underlying illness (Ambrosino *et al* 1995[10]; Meduri *et al* 1996[11]; Wood *et al* 1998[12]; Plant *et al* 2000-2001[5]; Carlucci *et al* 2003[13]; Nava and Ceriana 2004[6]; Girault *et al* 2009[14]; Carratu *et al* 2005[15]).

In the present study, NIV was observed to be successful in rapid and sustained improvement in gas exchange in 77.5% patients with type 2 respiratory failure and the endotracheal intubation could be avoided. The overall efficacy of NIV in avoiding intubation in this study is marginally more than the rate reported in published randomized studies[16-18].

We found a 22.5% rate of NIV failure in our population of patients with type 2 respiratory failure treated with NIV. These figures are at the lower end of the ones reported in other studies where NIV failure rate was between 9 and 50%.[19]

Determinants of outcomes of type 2 respiratory failure patients treated with NIV that we investigated and are common to other studies are initial arterial blood gases, age, and risk factors. The pH level has been reported to be a critical prognostic factor[1,20-23].

In the present study we took patients with initial pH range of 7.25-7.35. Patients with more severe acidosis pH<7.30 shown a poor outcome as compared to patients with pH 7.30-7.35.

In our study we took patients with type 2 respiratory failure with paCo2 >45 mm Hg and has shown that patients with initial PaCo2 between 60-80 mmHg reported better outcome as compared to patients with higher PaCo2 level (>80 mmHg).

Study by Brandao *et al* reported NIV improvement even at mean paCO2 of 75 mmHg[24].

Study by Steriade *et al* found that paCO2 after 1 hour of NIV is an independent predictor for NIV response[25].

Study by Poponick *et al* found no relationship between baseline parameters and the likelihood of success of NIV, but with the lack of change in blood gases after one hour trial being the best predictor for the need for ETI[26].

In our study, Patients failing on NIV have a significantly greater abnormality in PaCO2 and pH before starting NIV. Baseline pH is found to be able to predict success or failure of NIV (mean pH of 7.30 +/- 0.02 in success group vs. 7.27+/-0.02 in failure group).

In our study, it is difficult to draw meaningful conclusions on the outcome of NIV on low Pao_2 (<60 mm Hg).

Several studies found that hypoxemia was independently associated with NIV failure[27-30].

Strengths of the study

- The prospective nature of the study.
- The study sample which was relatively large when compared with some of the other Indian studies.
- Since it is a tertiary care center study the transition from non-invasive ventilation to invasive mechanical ventilation could be done easily.

Limitations of the study

The study did not have a control group which had impact on the statistical analysis of group differences.

Conclusion

Present study suggests that NIV is highly effective in treating patients with type 2 respiratory failure with pH 7.25-7.35. This study also shows that patients with, history of previous mechanical ventilation, high initial PaCo2 and low pH have lower chance of success with NIV.

Study indicates that a trial of NIV is effective in improving gas exchange, reducing intubation in patients with type 2 respiratory failure, suggesting that NIV is a safe and effective means of ventilator support for patients with type 2 respiratory failure. The study provides strong evidence for the use of NIV as a first line intervention in patients with type 2 respiratory failure.

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