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# Efficacy and Safety of Non-Invasive Ventilation for Post Extubation Respiratory Distress in Hypoxic and Hypercapnic Respiratory Failure

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## Abstract

**Background:** Respiratory distress after extubation with the need for reintubation is a common event. The act of reintubation is associated with numerous life-threatening complication and high mortality rate. The role of non-invasive ventilation (NIV) in patients who developed respiratory distress is not clear.

**Aim of the study:** To assess the effectiveness of non-invasive pressure support ventilation (NIPPV) in avoiding reintubation in patients who develop respiratory distress after extubation in hypoxic and hypercapnic patients.

**Patients and methods:** In this prospective observational study, one hundred and three patients with post extubation respiratory distress met our inclusion and exclusion criteria and were enrolled. NIPPV were applied to all patients and they were monitored for signs of failure of this technique and the need for reintubation. This cohort is further divided according to the initial cause of respiratory failure into hypoxic and hypercapnic groups. The primary outcome measure was the technique success rate to avoid reintubation; secondary outcome measures were ICU mortality, length of ICU stay.

**Results:** No statistically significant differences were observed in success rate, mortality and length of ICU stay between both groups.

**Conclusion:** The type of respiratory failure as a primary etiology for mechanical ventilation does not affect the success rate of the use of NIPPV in patients who developed post extubation respiratory distress.

**Keywords:** Post extubation respiratory distress; Non-invasive ventilation

## Introduction

Respiratory distress after extubation is a common event [1-4], and mortality rates of about 30 to 40% is associated with reintubation after extubation in those patients [3,5,6]. Several factors may contribute to extubation failure as: Upper airway obstruction [7,8], excess respiratory secretions [9,10], Inability to protect airway [11,12], cardiac failure or ischemia [13], encephalopathy[14], respiratory muscle load and capacity imbalance [15,16], gastrointestinal bleeding [4], sepsis [17,18], seizures [19], and the need for surgery [20].

The higher mortality rate observed with reintubation may be attributed to numerous complications associated with the act of reintubation itself [21,22], it may also be due to increased incidence of complications after reintubation [23-26], other studies suggests that there is no difference in mortality when comparing cohorts with and without complications after reinsertion of the endotracheal tube [27].

The use of noninvasive ventilation (NIV) instead of intubation in patients with acute respiratory failure has been used in a number of clinical situations. NIV has been established as a useful and safe method to improve gas exchange for acute respiratory failure patients with different etiologies [28,29].

It can be applied primarily to avoid endotracheal intubation in patients with acute respiratory failure [30-33], as an adjunct therapy to weaning from mechanical ventilation, preventively to all extubated patients or as a rescue therapy for patients who develop post-extubation respiratory distress (PERD) [34,35].

For patients who developed PERD, the role of NIV is still questionable and many studies were conducted to assess its efficacy but the results from these studies have shown conflicting outcomes. Moreover, the value of the use of this technique in different patient categories as in patients with different etiologies or in hypoxic versus hypercapnic patients is still unclear.

So we conduct this study to assess the effectiveness of non-invasive pressure support ventilation (NIPPV) in avoiding reintubation in patients who develop respiratory distress after extubation in two types of patients; hypoxic and hypercapnic respiratory failure.

The primary outcome was the technique success rate to avoid reintubation for 48 hours after development of PERD in each type; secondary outcomes included mortality rate and length of ICU stay.

## Patients and Methods

This observational prospective single center cohort study was performed in Assiut University Hospital. All consecutive patients who

met our inclusion and exclusion criteria were included in the study. The protocol of the study was approved by our local ethics committee and all patients or their relatives gave an informed consent before participation in this study.

## Patients

Patients were considered eligible for participation in this study if they had successful weaning and extubation followed by respiratory distress and the need for mechanical ventilation. Patients had to be intubated and mechanically ventilated for at least 48 hours prior to successful weaning and extubation. They also had to develop respiratory distress within 48 hours of this successful extubation.

Initial successful weaning were done with all patients met the following weaning criteria: arterial oxygen tension ($PaO_2$)/fraction of inspired oxygen ($FiO_2$) of not less than 150, PEEP of 5 cm $H_2O$, no vasopressor support, hemoglobin level of 10 gm/dl, no fever and no major electrolyte disturbances.

Exclusion criteria were patients' refusal, uncooperative patients, hemodynamic instability, ineffective cough, swallowing disorders, neuromuscular disorders, excessive bronchial secretions and disturbed conscious level.

## Non-invasive ventilation after development of PERD

Standard medical respiratory therapy was started immediately to respiratory distressed patients in the form of physiotherapy, mucolytics, and bronchodilators as inhaled β-agonists and inhaled ipratropium bromide as clinically indicated. Other medical treatments were optimized by the attending physician according to the cause of respiratory failure and other medical conditions.

NIPPV was delivered through full-face mask in pressure support ventilation (PSV) mode with pressure support of 10 cm $H_2O$ and PEEP of 5-7 cm $H_2O$ which may be gradually increased to 12 cm $H_2O$ as needed. The level of pressure support was adjusted for each patient to obtain an exhaled tidal of ≥ 5 ml/kg and respiratory rate ≤ 25 breaths/minute. The $FiO_2$ and PEEP was titrated to maintain $PaO_2$ of more than 60 mmHg.

Patients were evaluated every morning by allowing them to breathe supplemental oxygen through Venturi mask with $FiO_2$ of 0.4 with interruption of the NIPPV. If patients did not meet the discontinuation criteria as then NIPPV applied again. Criteria for discontinuation of NIPPV included respiratory and hemodynamic stability, respiratory rate less than 35 breath/min, accepted arterial blood gas (ABG), with $PaO_2$ more than 60 mmHg, $PaCO_2$ less than 60 mmHg and pH more than 7.35.

Reintubation of these patients was considered with:

1. Respiratory arrest or signs of respiratory instability appeared as tachypnea, cyanosis, respiratory acidosis, gasping for air and use of accessory muscles of respiration.

2. Cardiac arrest or occurrence of severe hemodynamic instability with no response to fluids or vasoactive drugs,

3. Deterioration of conscious level.

4. Patient intolerance to NIPPV.

## Data collection

On admission, demographic data, acute physiology and chronic health evaluation (APACHE) II score and cause of respiratory failure were recorded. On randomization we collect the previous duration of mechanical ventilation, the time elapsed from extubation till occurrence of PERD, the physiologic parameters and ABG just before application of NIPPV. At the end we recorded the technique success rate, the ICU length of stay and ICU mortality.

## Statistics

The cohort of the study was divided according to the primary cause of respiratory failure into type I and type II. Data were analyzed with the statistical package SPSS v21, and was shown as mean (SD), ratios and percentages as appropriate. For group comparison, qualitative or categorical variables were compared by $Chi^2$ or Fisher's exact test as appropriate. Quantitative continuous variables were compared by independent Student t test or Mann-Whitney nonparametric test as appropriate. The level of significance was set at 0.05.

## Results

In a two-year period of the study, 578 patients were mechanically ventilated in our respiratory, trauma and postoperative ICUs. One hundred and thirty one patients had PERD, but 28 patients did not meet our inclusion and exclusion criteria. Therefore, 103 patients were included in the study. We further subdivided these patients according to the etiology of respiratory failure into hypoxic group and hypercapnic group (Figure 1).

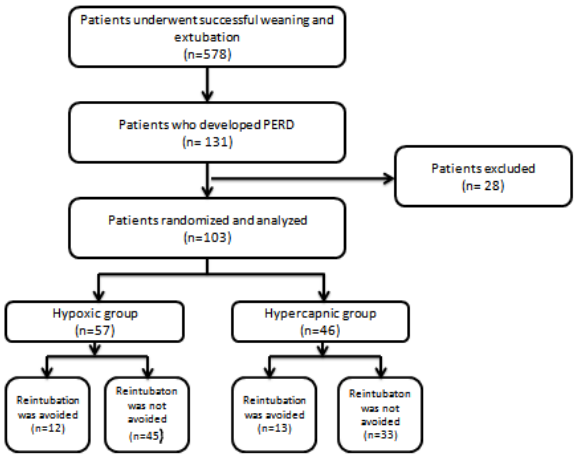


**Figure 1:** Flow chart of the trial.

Patients' general characteristics were summarized in Table 1. There were no significant differences observed between both groups.

Baseline physiologic parameters and ABG analysis were recorded just before use of NIPPV to treat PERD, group I showed significantly higher baseline respiratory rate, and pH, and significantly lower $PaO_2$, $PaO_2$/ $FiO_2$ ratio, arterial $CO_2$ tension, bicarbonate level and base excess. Both groups were comparable as regard heart rate, mean arterial blood pressure and temperature (Table 2).

| | Hypoxic group n=57 | Hypercapnic group n=46 | p-value |
|---|---|---|---|
| Gender (M/F) | 35/22 | 33/13 | 0.186 |
| Age (years) | 46.94 ± 13.73 | 54.71 ± 15.12* | 0.007 |
| Weight (Kg) | 84.64 ± 6.86 | 85.02 ± 5.78 | 0.769 |
| Height (cm) | 166.4 ± 4.25 | 166.6 ± 5.37 | 0.829 |
| APACHE II score | 38.12 ± 9.52 | 36.56 ± 10.06 | 0.423 |
| Previous duration of mechanical ventilation (days) | 5.94 ± 3.97 | 5.32 ± 4.16 | 0.442 |
| Time to PERD (hours) | 9.15 ± 3.59 | 8.3 ± 4.85 | 0.308 |
| Data are represented as mean ± SD unless otherwise indicated; *P value <0.05 | | | |

**Table 1:** Group characteristics.

| Parameter | Hypoxic group n=57 | Hypercapnic group n=46 | p-value |
|---|---|---|---|
| Respiratory rate | 32.98 ± 5.55 | 29.95 ± 4.23* | 0.003 |
| Heart rate | 109.7 ± 11.39 | 113.67 ± 15.23 | 0.133 |
| Mean arterial blood pressure | 99.24 ± 17.12 | 102.28 ± 15.35 | 0.351 |
| Temperature | 37.78 ± 0.69 | 37.76 ± 0.7 | 0.894 |
| pH | 7.5 ± 0.06 | 7.37 ± 0.03* | 0 |
| Arterial $O_2$ tension | 69.57 ± 5.83 | 71.68 ± 4.26* | 0.042 |
| $PaO_2$/ $FiO_2$ ratio | 120.74 ± 24.93 | 170.12 ± 23.83* | 0 |
| Arterial $CO_2$ tension | 32.65 ± 5.72 | 59.02 ± 6.49* | 0 |
| $HCO_3$ level | 25.21 ± 2.17 | 33.55 ± 2.69* | 0 |
| Base excess | 2.17 ± 2.28 | 8.08 ± 2.57* | 0 |
| Data are represented as mean ± SD; *P value <0.05 | | | |

**Table 2:** Some physiologic and ABG data just before NIPPV.

As regard technique outcome (Table 3), 12 patients out of 57 in group I have successful weaning course, they represented about 21.05% of all cases in this group.

| | Hypoxic group n=57 | Hypercapnic group n=46 | p-value |
|---|---|---|---|
| Technique success rate | 12 (21%) | 13 (28%) | 0.489 |
| Length of ICU stay (days) | 13.56 ± 8.35 | 12.02 ± 7.89 | 0.343 |
| ICU mortality | 14 (25%) | 9 (20%) | 0.637 |
| Data are represented as mean ± SD or number (%) | | | |

**Table 3:** Post-technique outcome of patients' status.

. In group II 13 patients out of 46 had this successful course and they represented about 28.26% with no significant differences between both groups. Length of ICU stay was comparable in both groups, 13.56 (8.35) days versus 12.02 (7.89).

The ICU mortality was 14 out of 57 patients (24.56%) in group I and 9 out of 46 patients (19.57%) in group II with no significant differences between both groups.

## Discussion

The present results demonstrated that hypoxic or hypercapnic types of respiratory failure as a primary pathology for initial mechanical ventilation does not affect success rate when NIPPV is used to avoid reintubation in patients who developed PERD, neither the length of ICU stay nor the ICU mortality was affects by the initial type of respiratory failure. The difference in the baseline ABG values just before the use of NIPPV were expected due to the different initial pathology of both groups.

Fewer studies published testing the use of NIPPV to avoid post-extubation reintubation in patients who developed respiratory distress. Instead, the majority of studies examining NIV have assessed its role in averting the need for primary endotracheal intubation in patients with acute respiratory failure [30-33]. These studies showed that NIV is effective in reducing morbidity and mortality in patients with acute-on-chronic respiratory failure; but that the benefit in patients with hypoxemic respiratory failure is less clear [36].

Earlier studies examining the effect of NIPPV to avoid reintubation showed some positive results. Chiang and Lee [37] who put 19 patients with respiratory distress on NIPPV with Bi-level and after 58% success rate, they suggest that NIPPV via nasal mask may be considered as an alternative to endotracheal intubation. In 1999 Munchi et al. [38] reached a success rate of 72% in their study using non-invasive CPAP or Bi-level.

The above positive results were antagonized by the work of Keenan et al. [39] who studied the use of NIPPV for PERD compared to standard-therapy group; they found no difference in the rate of reintubation or hospital mortality or the duration of mechanical ventilation or length of ICU or hospital stay. They concluded that even the addition of NIPPV to standard medical therapy does not improve outcome in heterogeneous groups of patients who develop respiratory distress during the first 48 hours after extubation.

And again in their multicenter study Esteban et al., in 2004 [40] evaluated the role of non-invasive ventilation in PERD. They studied 221 patients in 37 centers over 8 countries. Extubated patients who develop respiratory failure within 48 hours after at least 48 hours of mechanical ventilation were randomly assigned to either NIPPV by face mask or standard medical therapy. Out of 114 patients assigned for non-invasive therapy and 107 patients assigned to standard medical therapy, rate of reintubation was 48 % in both groups. The rate of death in the intensive care unit was higher in the NIV group than in the standard-therapy group. The median time from respiratory failure to reintubation was longer in the NIV group. They concluded that NIPPV does not prevent the need for reintubation or reduce mortality in unselected patients who have respiratory failure after extubation.

Agarwal et al., [41] carried out another multicenter study and suggested that NIPPV should be used judiciously, if at all, in patients with PERD, but it appears to be promising as a prophylaxis to prevent re-intubation in patients "at risk" for developing PERD.

Mixed patients in all above studies may account for these variable results and perhaps patient selection may improve the results of NIPPV, some criteria thought it may change these results, first was the application of the NIPPV in COPD patients, second its application in cardiac patients and in third in post-surgical patients.

Krishna et al., [42] in their meta-analysis study performed a multi-regression analysis to demonstrate the effect of the above criteria as predictor factors for success of NIPPV. They found no effect of all criteria as predictors of success in PERD, according to the authors these results may be explained by the relatively small number overall of COPD (17.95%) and cardiac failure (14.5%) patients.

In our study we tried to compare the effect of the type of respiratory failure on the success rate with comparable percentages of both types, but we obtained the same results with no effect of the type of respiratory failure on the rate of reintubation as a primary outcome.

We should be cautious with generalization of the results of the present study to general practice. The timing of application of the NIPPV as by choosing different criteria for respiratory distress may affect the outcome, the interface used for the application, and the mode of NIPPV may also be factors that affect the outcome.

## Conclusion

We concluded that the type of respiratory failure as a primary etiology for mechanical ventilation does not affect the success rate of the use of NIPPV in patients who developed PERD.

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