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The risk factors for late failure of non-invasive mechanical ventilation in acute hypercapnic respiratory failure

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SUMMARY

The risk factors for late failure of non-invasive mechanical ventilation in acute hypercapnic respiratory failure

Introduction: Non-invasive mechanical ventilation provides early improvement in most of the patients with acute hypercapnic respiratory failure. The aim of our study was to determine the risk factors for late failure of non-invasive mechanical ventilation in patients with acute hypercapnic respiratory failure.

Materials and Methods: Ninety three patients were prospectively evaluated. Non-invasive mechanical ventilation was accepted to be successful if the patient was discharged from the hospital without the need for intubation (group 1) and to be late failure if a deterioration occurred after an initial improvement of blood gases tension and general conditions (group 2).

Results: Non-invasive mechanical ventilation was successful in 62 (66.7%) patients. In 25 (26.9%) patients a late failure was observed. There was no difference between groups 1 and 2 in terms of pretreatment pH, PaCO₂ and PaO₂/FiO₂. However, serum C-reactive protein level, Acute Physiology and Chronic Health Evaluation II (APACHE II) score and frequency of bronchiectasis and pneumonia were significantly higher and serum albumin level, Glasgow Coma Score, cough strength and compliance to non-invasive mechanical ventilation were significantly lower in group 2.

Conclusion: The pretreatment high APACHE II Score and C-reactive protein level, low Glasgow Coma Score, albumin level, cough strength, bad compliance to non-invasive mechanical ventilation, the presence of bronchiectasis and pneumonia and absence of significance improvement in PaO₂/FiO₂ after treatment were determined as risk factors for non-invasive mechanical ventilation late failure.

Key words: Acute hypercapnic respiratory failure, mechanical ventilation, non-invasive mechanical ventilation, respiratory failure, respiratory intensive care unit

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ÖZET

Akut hiperkapnik solunum yetmezliğinde noninvaziv mekanik ventilasyonun geç başarısızlığı için risk faktörleri

Giriş: Noninvaziv mekanik ventilasyon akut hiperkapnik solunum yetmezlikli hastaların çoğunda erken düzelme sağlar. Bu çalışmada amacımız, akut hiperkapnik solunum yetmezlikli hastalarda noninvaziv mekanik ventilasyonun geç başarısızlığı için risk faktörlerini saptamaktır.

Materyal ve Metod: Doksan üç hasta prospektif olarak değerlendirildi. Noninvaziv mekanik ventilasyon, hastanın entübasyon ihtiyacı gelişmeden hastaneden taburcu olması halinde başarılı (grup 1), kan gazlarında ve genel durumunda başlangıçta düzelme sonrası kötüleşme görülmesi halinde ise geç başarısız olarak kabul edildi (grup 2).

Bulgular: Noninvaziv mekanik ventilasyon 62 (%66.7) hastada başarılıydı. 25 (%26.9) hastada geç başarısızlık gözlemlendi. Tedavi öncesi pH, PaCO₂ ve PaO₂/FiO₂ açısından grup 1 ve grup 2 arasında farklılık yoktu. Ancak, serum C-reaktif protein düzeyi, Akut Fizyolojik ve Kronik Sağlık Değerlendirme II (APACHE II) skoru, bronşiektazi sıklığı ve pnömoni anlamlı olarak daha yüksekti ve serum albumin düzeyi, Glasgow koma skalası, öksürük gücü ve noninvaziv mekanik ventilasyon kompliyansı grup 2'de anlamlı olarak daha düşüktü.

Sonuç: Tedavi öncesi yüksek APACHE II skoru ve C-reaktif protein düzeyi, düşük Glasgow Koma Skalası, albumin düzeyi, öksürük gücü, noninvaziv mekanik ventilasyona kötü kompliyans, bronşiektazi ve pnömoni varlığı, tedavi sonrası PaO₂/FiO₂'de anlamlı düzelme olmaması noninvaziv mekanik ventilasyon geç başarısızlığı için risk faktörü olarak saptandı.

Anahtar kelimeler: Akut hiperkapnik solunum yetmezliği, mekanik ventilasyon, noninvaziv mekanik ventilasyon, solunum yetmezliği, solunum yoğun bakım ünitesi

INTRODUCTION

In recent years non-invasive mechanical ventilation (NIMV) has been successfully used in selected populations as an effective treatment for acute hypercapnic respiratory failure (AHRF). Non-invasive mechanical ventilation improves alveolar ventilation, gas exchange abnormalities and respiratory rate in most patients with AHRF. With its low complication rate, it also shortens mechanical ventilation time and intensive care unit (ICU) stays (1,2). Despite recent encouraging results, NIMV is not always successful in the management of AHRF. The NIMV failure eventually requires intubation. The most significant success indicators of NIMV are decrease in the respiratory rate and PaCO₂, improvement in pH and oxygenation in the first two hours of NIMV (3). The NIMV failure rate is in the range of 5-40% in the literature (4-11).

In a subgroup of patients, despite an initial improvement in arterial blood gases and clinical condition, a late failure (> 48 hours) characterized with deterioration after an initial success may occur. The recognition of this subset of patients is critical because prolonged treatment of NIMV may result in a delay in the time of intubation and increased mortality. Although, the factors associated with NIMV failure have been well established, the risk factors for late failure of NIMV and the clinical and physiological characteristics of these patients has been evaluated in only a few studies (12,13).

In this study, we aimed to establish the effectiveness of NIMV and risk factors related with late failure of NIMV in patients with AHRF.

MATERIALS and METHODS

The study was performed in a respiratory ICU of tertiary-care university teaching hospital. The study protocol was approved by the local ethics committee. Informed consent was obtained from the patients or the first-degree relative. Patients who were admitted with AHRF were enrolled to study and evaluated prospectively. Acute hypercapnic respiratory failure was defined as; as severe dyspnea, hypercapnia (PaCO₂> 45 mmHg) and acute respiratory acidosis (pH< 7.35). Patients who had contraindications for NIMV [respiratory or cardiac arrest, medical instability (hypotensive shock, myocardial infarction, uncontrolled ischemia or arrhythmia), inability to protect airways, untreated pneumothorax, mask unsuitability, (facial surgery, trauma, deformity or burn), recent upper airway or oesophageal surgery] were excluded from the study.

The demographical data and diagnoses of the patients were recorded. Also, strength of cough (0: too weak, 10: strongest), secretion quantities (0: none, 10: plenty) and patient's compliance score to NIMV (1= poor, 2= quite bad, 3= sufficient, 4= good, 5= excellent) were evaluated by the Likert scale. Respiratory rate, heart rates, blood pressure values, complete blood count, blood biochemistry, C-reactive protein (CRP), Glasgow Coma Score (GCS) and Acute

Physiology and Chronic Health Evaluation II (APACHE II) score were recorded. The presence of bronchiectasis and pneumonia were investigated by radiologic evaluation.

All patients received standard medical treatment with oxygen by nasal cannula to maintain arterial saturation at approximately 90%, mucolytics and antibiotics if needed. Chronic obstructive pulmonary diseases (COPD) patients also received inhaled steroids, bronchodilators and oral steroids (for one week) and teophylline. Patients were ventilated with NIMV using a full face mask. The inspiratory positive airway pressure (IPAP) was adjusted according to patient's tolerance to obtain a tidal volume of 7-10 mL/kg with an expiratory positive airway pressure (EPAP) lower than 7 cmH₂O. The EPAP was set initially at 5 cmH₂O and increased in increments of 1 cmH₂O until fractional inspired oxygen (FiO₂) requirement was less than 0.5. The respiratory count, heart rate, systolic and diastolic blood pressures, arterial blood gases were evaluated in the 1st and 3rd hours of the treatment.

For associated complications, factors reported by Jimenez et al. were used (14). The complications of NIMV were also recorded.

While the success of NIMV was defined as absence of death or need of intubation with the patient's discharge from hospital (group 1), late failure (after > 48 hours of NIMV) was defined as deterioration occurred after an initial improvement of blood gas tension and general condition (group 2). At the time of late failure, patients in group 2 were still receiving NIMV. Early failure of NIMV was defined as death or need of intubation after a few hours of NIMV and this group was not included in the comparison. The need of intubation was defined as presence of one of following criteria: (1) pH below 7.20, (2) pH: 7.20-7.25 on two occasions 1 h apart, (3) hypercapnic coma (GCS< 8 and PaCO₂> 8kPa) (4), PaO₂ below 6 kPa despite maximum tolerated FiO₂ and (5) cardiorespiratory arrest.

Statistical Analysis

The SPSS 11.5 package program was used in the analysis of the data. As a defining measure, the average standard deviation [median (min-max)] was used in the variables acquired using measures, and the frequency (%) was used in the variables acquired using a count. For comparisons between the groups, the Kruskal-Wallis variance analysis was used, while within the groups, the Friedman test was used. A p value of less than 0.05 was considered as statistically significant.

RESULTS

Ninety three patients with AHRF, with a mean age of 67.70 (median 69 ± 11.97 years), admitted to ICU were enrolled to study. The diagnoses in both groups were showed in Table 1. 73 (78.5%) of 93 patients had comorbid diseases. There were no significant differences in term of comorbid diseases between two groups. The baseline characteristics of study group were shown in Table 2.

While NIMV was successful in 62 (66.7%) patients, in 6 patients early failure and in 25 (26.9%) patients late failure was observed. The mean time of late failure was 6.3 days (median 4.50 ± 4.66). The comparison of groups regarding baseline features were showed in Table 3. There was no difference between groups 1 and 2 in terms of pretreatment pH, PaCO₂, PaO₂/FiO₂, respiratory rate, heart rate, and systolic and diastolic blood pressures. However, serum CRP level, APACHE II score were significantly higher and serum albumin level and GCS were significantly lower in group 2. The presence of bronchiectasis and pneumonia was significantly higher in group 2. The cough strength and compliance to NIMV score were significantly higher in group 1. The amount of secretion was higher in group 2, but the difference was not significant. The compliance score and cough strength which were evaluated by Likert scale were significantly lower in group 2.

Table 1. The diagnoses of patients

Diagnoses	Group 1		Group 2		Total	
	n	%	n	%	n	%
COPD	45	72.6	19	76	67	72.1
Obesity-hypoventilation syndrom	12	19.4	1	4	13	14.0
Kyphoscoliosis	5	8.1	1	4	7	7.5
Interstitial lung disease	0	0	4	16	6	6.5
Total	62	100	25	100	93	100.0

* COPD: Chronic obstructive pulmonary disease.

Table 2. Characteristics of the study group before treatment

n	91
Total protein (g/dL)	6.65 ± 0.84
Albumin (g/dL)	3.55 ± 0.79
CRP (mg/dL)	9.44 ± 21.93
APACHE II	18.98 ± 4.53
GCS	14.19 ± 2.04
Body mass index	28.19 ± 8.47
Heart rate (/min)	99.67 ± 20.25
Respiratory rate (/min)	27.12 ± 8.46
pH	7.28 ± 0.53
PaCO ₂ (mmHg)	67.26 ± 12.06
PaO ₂ /FiO ₂	150.53 ± 70.34

CRP: C-reactive protein, APACHE II: Acute Physiology and Chronic Health Evaluation II, GCS: Glasgow Coma Score.

There was no significant difference for baseline pH and PaCO₂ between two groups. Also, after 1 h and 3 h of NIMV a significant improvement was observed in both groups. Similarly, the respiratory rate was significantly decreased in both groups after 1 h and 3 h of NIMV. While a significant decrease in heart rate after 1 h and 3 h of NIMV was observed in group 1, there was no significant change in group 2 (p: 0.003 and 0.881, respectively). Also, after 1 h and 3 h of

NIMV, a significant increase in the PaO₂/FiO₂ value was observed in group 1 (p: 0.01), however there was no significant change in group 2 (p: 0.79).

For associated complication, before treatment, there was no significant difference between group 1 and group 2 (19.4% vs. 32%, respectively; p: 0.11). However, after NIMV there was significantly higher associated complications in group 2 (13.3% vs. 44%, respectively; p: 0.004).

DISCUSSION

In recent years, NIMV has been shown to be effective in certain types of acute respiratory failure, based on the results of clinical trials showing improved outcomes. However, NIMV is not always successful and selection of appropriate patients is crucial for the optimization of NIMV success rates. Predictors of NIMV success or failure may be helpful in selecting patients and the reported best predictors of success of NIMV are reduction in respiratory rate, improvement in pH, oxygenation and PaCO₂ within one to two hours. The pretreatment high APACHE II score, CRP level and low GCS were also reported as predictive factors for NIMV failure (15). In some patients, despite an initial improvement, after > 48 hours of NIMV a deterioration which is defined as late failure may be

Table 3. The comparison of groups regarding baseline features

	Group 1	Group 2	p
n	62	25	
Age	67.63 ± 12.13	69.70 ± 11.8	0.082
Bronchiectasis (present/absent)	9/53	10/15	0.019
Pneumonia (present/absent)	19/43	16/9	0.007
Strength of cough	4.95 ± 2.38	3.04 ± 2.23	0.000
Compliance to NIMV	3.63 ± 1.07	2.84 ± 1.28	0.000
Comorbid diseases (present/absent)	49/13	22/3	0.115
Secretion Quantity	2.29 ± 2.01	2.92 ± 2.77	0.060
Total protein (g/dL)	6.76 ± 0.79	6.38 ± 0.93	0.210
Albumin (g/dL)	3.70 ± 0.86	3.22 ± 0.55	0.006
CRP (mg/dL)	5.86 ± 0.77	18.10 ± 40.06	0.010
APACHE II	17.35 ± 3.70	21.44 ± 4.48	0.000
GCS	14.65 ± 1.13	13.12 ± 3.28	0.000
Body mass index	29.34 ± 9.05	26.29 ± 7.28	0.163
Heart rate (/min)	98.19 ± 19.93	101.40 ± 19.01	0.477
Respiratory rate (/min)	25.94 ± 7.64	28.08 ± 8.70	0.073
pH	7.29 ± 0.04	7.27 ± 0.06	0.060
PaCO ₂ (mmHg)	66.39 ± 10.67	69.39 ± 15.32	0.804
PaO ₂ /FiO ₂	147.55 ± 65.72	165.17 ± 85.83	0.330

NIMV: Non-invasive mechanical ventilation, CRP: C-reactive protein, APACHE II: Acute Physiology and Chronic Health Evaluation II, GCS: Glasgow Coma Score.

developed. There is little data in the literature about the clinical and physiological characteristics of these patients and the risk factors for late failure of NIMV.

In a multicentre randomised study comparing NIMV with standart treatment protocols in patients with COPD, it was shown that the use of NIMV significantly reduced the need for endotracheal intubation; however, 15% of patients who were successfully treated with NIMV initially, needed endotracheal intubation after at least 48 hours (16). In another study performed by Meduri et al, NIMV was applied in 158 patients with ARF (1). NIMV was effective in improving or correcting gas exchange abnormalities in 80% of patients and avoiding endotracheal intubation in 65%. However, 28% of the initial responders needed endotracheal intubation and the mortality rate in this subgroup was 22%. The characteristics of this subset of patients were not determined in both of these two studies. There are only a few studies evaluating factors related with late failure of NIMV. Moretti et al, studied 186 patients with COPD treated with NIMV because of AHRF (12). In their study, 74% of patients were successfully ventilated non-invasively at first and were therefore enrolled for data analysis. The authors found that, after 8.4 days (range 3-13) days of NIMV 23% of patients experienced a new episode of acute respiratory failure. The occurrence of late NIMV failure was significantly associated with functional limitations before admission to the respiratory ICU, the presence of medical complications and a lower pH on admission. They also reported that, these patients have a very poor in hospital prognosis, especially if NIMV is continued rather than prompt initiation of invasive ventilation. In another study, performed by Carratu et al, in which 122 patients with COPD complicated by ARF and treated with NIMV were enrolled, 10 (8%) patients had a late failure (13). This subgroup of patients had poor prognosis with a 80% mortality. The authors reported that the characteristics of the late failure patients group were very similar to the success group without any statistically significant difference and the only predictor of late failure was the presence of metabolic disorders. They also reported that, the early failure group had different characteristics owing to more severe conditions with higher values of APACHE II score and lower values of pH and GCS.

In our study, the rate of late failure was 26.9%, quite similar with Meduri's and Moretti's study and higher than Brochard's and Carratu's study (1,12,13,16). Although majority of patients had a diagnosis of COPD, our study consisted of a heterogenous popu-

lation with different etiology of AHRF different from previous studies. However, we couldn't compare NIMV success and factors related with failure between each disease due to small number of patients with non-COPD diseases. As mentioned previously, little is known about characteristics of late failure patients. In our study, pretreatment high serum CRP level, APACHE II score, presence of bronchiectasis and pneumonia, low GCS, cough strength and compliance to NIMV and no improvement in $\text{PaO}_2/\text{FiO}_2$ after NIMV, were found as risk factors for late failure of NIMV. Also, before treatment, although there was no significant difference between group 1 and group 2 for associated complication, after NIMV there was significantly higher associated complications in group 2. In contrast, in Meduri's study, functional limitations before admission to the respiratory ICU, the presence of medical complications and a lower pH on admission and in Carratu's study, only the presence of metabolic disorders were reported as risk factors for late failure. Different from Meduri's report, in our study, there was no difference between success and late failure groups in terms of pretreatment pH and PaCO_2 similar with Carratu's study.

Although little is known about the clinical and physiological characteristics of patients with late failure, it has been reported that these patients have a very poor prognosis with high mortality and this high mortality may be due to prolonged application of NIMV and a delay in intubation. Moretti et al, reported that, late failure of NIMV has a high mortality rate (67.7%) which was significantly higher if the NIMV is maintained (91.6%) than if the patient was given invasive ventilation (52.6% mortality) (12). In our study the mortality rate in late failure group was found as 73.3% consistent with previously reported poor prognosis.

CONCLUSION

In conclusion, the principal finding of our study was pretreatment high APACHE II score and CRP level, low GCS, albumin level, cough strength, bad compliance to NIMV, the presence of bronchiectasis and pneumonia and absence of improvement in $\text{PaO}_2/\text{FiO}_2$ after treatment are predictors of NIMV late failure.

AUTHORS' CONTRIBUTION

AÇ, AK, ÖED designed and performed study, collected data and wrote the paper. ZPÖ, EŞ, NDF collected and analyzed data and helped to write the paper.

CONFLICT of INTEREST

None declared.

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