Does the Body Mass Index Affect the Success of Noninvasive Mechanical Ventilation in Patients with Acute Hypercapnic Respiratory Failure?

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Abstract

Objective: Obesity has many negative effects on lung functions. It is not yet clear whether body mass index (BMI) affects the success of noninvasive mechanical ventilation (NIMV). The aim of this study was to investigate the differences in NIMV strategies, on the basis of BMI, in patients with acute hypercapnic respiratory failure and the effect of BMI on the success of NIMV.

Methods: A total of 86 patients who had acute hypercapnic respiratory failure were enrolled consecutively. They were grouped according to BMI as follows: BMI 18.5 - 24.9kg/m^2 (normal); group 1, BMI 25 - 30kg/m^2 (overweight); group 2, BMI>30kg/m^2 (obese); group 3. Age, gender, duration of ICU stay, pressures of NIMV and Arterial Blood Gas (ABG) before, during and after the NIMV were recorded.

Results: In total, 52 patients (60%) were male. The mean age of the patients was 70 ± 12 years. The success rates of NIMV in groups 1, 2 and 3 were 50%, 28% and 21%, respectively. The success rates were not significantly different between groups (p=0.79). In group 3, the respiratory rate was higher and pH was lower during the first hour compared to the other groups (p<0.05, p<0.05). PaCO$_2$ levels were higher in group 3 on the first day and at the end of NIMV treatment (p=0.04, p<0.05).

Conclusion: NIMV strategies should be different in acute hypercapnic respiratory failure patients with a high BMI, and in these patients, clinical improvement requires a long duration.

Keywords

Hypercapnic respiratory failure, NIMV, BMI

Introduction

Noninvasive Mechanical Ventilation (NIMV) application strategies and the factors affecting its success are still highly disputed issues. In acute and chronic respiratory failure cases, which may develop in association with different etiologies, there have been many studies concerning the applied NIMV methods and their results [1,2]. Among the factors concerning the patient, age and comorbid diseases (cardiovascular diseases, immunosuppression, pneumonia etc.) have been the most commonly emphasized [1]. However, few studies have investigated the influence of body weight or that of body mass index (BMI) in acute respiratory failure on NIMV.

In patients with chronic respiratory failure, it has been observed that lower BMI can lead to the impairment of pulmonary functions and the reduction of NIMV efficiency [3]. However, the effects of higher BMI in NIMV application are still not clearly known. Obesity (BMI>30kg/m^2) has become an important health problem, affecting 312 million people in developed and developing countries, and its prevalence in intensive care units has been substantially increasing [4,5]. There is obesity in 18% of the patients with chronic obstructive pulmonary disease (COPD) and in 16% to 24% of the patients with other respiratory failures [3].

Obesity has important effects on pulmonary functions and the functioning of other systems. Direct and indirect relationships between obesity and Obesity Hypoventilation Syndrome (OHS), Obstructive Sleep Apnea Syndrome (OSAS), postoperative acute respiratory failure and other medical problems have been demonstrated [6]. These patients are usually admitted to an intensive care unit for various reasons, such as hypercapnic respiratory failure, cor pulmonale, COPD attack, asthma attack, and pulmonary embolism [6,7]. The optimal mechanic ventilation methods applied in the intensive care unit are usually not used. The aim of the study was to investigate the effect of the BMI on the success of NIMV in patients with acute hypercapnic respiratory failure.

Materials and Methods

The patients who admitted to the respiratory care unit of Atatürk Chest Disease and Thoracic Surgery Training and Research Hospital between December, 2011 and March, 2013 and had acute hypercapnic respiratory failure were included. This study was planned as a retrospective cohort study. The required approval of the local ethics committee was obtained before beginning the study. The cases were divided into three groups as follows: Group 1 was composed of subjects with normal weight BMI between 18.5 - 24.9kg/m^2, Group 2 was formed composed of overweight patients with BMI between 25 - 30kg/m^2, and Group 3 was composed of obese patients with BMI greater than 30kg/m^2.

Table 1: Obstructive sleep apnea syndrome (OSAS) definition according to American Academy of Sleep Medicine Task Force.

OSAS was diagnosedto have fulfilled criteria A or B and criterion C, as defined below:

A) Excessive daytime sleepiness that is not better explained by other factors;

B) Two or more of the following symptoms that cannot be better explained by other factors: choking or gasping during sleep, recurrent awakenings from sleep, non-refreshing sleep, daytime fatigue, or impaired concentration;

C) Overnight monitoring demonstrating five or more obstructed breathing events per hour during sleep. If the patient did not undergo a polysomnograph, s/he was diagnosed clinically as having OSAS using criteria A and B.

Inclusion criteria

Patients who had acute hypercapnic respiratory failure (pH<7.35 and PaCO$_2$>45mmHg in ABG analysis, respiratory rate>25 per minute) were included in the study.

Exclusion criteria

Patients with malignancy or terminal respiratory disease, loss of conscious or clouding of consciousness (except hypercapnic encephalopathy), respiratory and/or cardiac arrest, intense secretion, agitation and lack of cooperation, unstable clinical condition (hypotensive shock, cardiac ischemia), trauma, burns, anatomic disorders of the face that would prevent a mask from being secured, impaired cough and swallowing reflex, and pure hypoxemic failure (PaO$_2$<60mmHg and PaCO$_2$<45mmHg in ABG analysis) were excluded from the study.

Definition criteria

Acute hypercapnic respiratory failure was defined to be present if PaO$_2$ was <60mmHg when patients received oxygen therapy and PaCO$_2$>45mmHg and pH<7.35.

OSAS was defined according to American Academy of Sleep Medicine Task Force (Table 1) [8].

Overlap syndrome was defined as the combination of COPD and sleep apnea- hypopnea syndrome [9]. COPD was defined according to the GOLD criteria [10].

Age, gender, APACHE II score, serum C-reactive protein (CRP) level, respiratory rate, intubation, mortality, lengths of stay in intensive care unit, lengths of stay in hospital, diagnoses, comorbid diseases, sessions of NIMV application, inspiratory positive airway pressure (IPAP), expiratory positive airway pressure (EPAP), initial, first hour-, fourth hour-, twenty fourth hour- ABG and the ABG values during discharge from the intensive care unit of all cases included into the study were recorded. The patients that had one major criterion (fever>38°C, cough, purulent sputum) or two minor criteria (dyspnea, chest pain, pulmonary consolidation evidence in physical examination, leukocyte counts >12000mm^3 or <4000mm^3) consistent with pneumonia, together with infiltration evidence in X-ray images, were considered as having pneumonia [11].

The failure of NIMV was determined in cases with 1 major or 2 minor criteria within the first hour of NIMV. The major criteria were considered to be respiratory arrest, loss of consciousness, psychomotor agitation necessitating sedation, impaired hemodynamics (systolic blood pressure <70mmHg or >180mmHg), and bradycardia (HR<50 beats/min). The minor criteria were a RR of >35/min that was also higher compared to the rate recorded at the time of initial presentation, arterial pH <7.30 that was also lower compared to the initial presentation, PaO$_2$<45mmHg despite oxygen support, and absence of a cough reflex that would clear secretions.

To use the APACHE II score system, the admittance of the patients to the intensive care unit (ICU), ABG analysis, biochemistry, hemogram, arterial blood pressure, body temperature, Glasgow Coma Scale (GCS), respiratory rate (RR) and heart rate (HR) were recorded.

NIMV application was performed through BiPAP Vision (BiPap® Vision, Respironics, USA) by using an oronasal mask of standard dimensions such that it covered the nose and the mouth. At the beginning, expiratory positive airway pressure (EPAP) was adjusted as 5cm H$_2$O and Inspiratory Positive Airway Pressure (IPAP) was adjusted to 10cm H$_2$O in pressure-support mode. As the cases improved according to the alterations in blood gas, the pressures were increased to 1 to 2cm H$_2$O. Back-up rate was adjusted in the beginning of the NIMV, it was not manipulated during treatment. Additionally, medical treatment appropriate to their diagnoses was administered.

Statistical Analysis

Data analysis was performed with the SPSS for Windows 15 software package. Descriptive statistics were summarized in a table by determining the means and standard deviations.

The Kruskal Wallis test was used for the comparison of ventilator parameters and ABG values. The Chi-Square test was used in the comparison of mortality, intubation, length of stay in the hospital, and length of stay in the Intensive Care Unit between groups. In the patients with successful NIMV, the Chi-Square test and Mann-Whitney U test were used in the comparison of differences in terms of pneumonia, diagnosis of OSAS, APACHE II score, and CRP level. The t-test was used in the comparison of diagnosis ratios between groups. The results were considered to be statistically significant when p<0.05.

Results

A total of 310 patients were accepted to the ICU of Atatürk Chest Disease and Thoracic Surgery Training and Research Hospital between December, 2011 and March, 2013. A hundred and ten patients had acute hypercapnic respiratory failure. Of these, 86 patients who had acute hypercapnic respiratory failure were included in the study. Twenty-four patients were excluded (5 patients had agitation and lack of cooperation, 7 had malignancy, 2 had anatomic disorders of face, 6 had intense secretion and 4 of them had respiratory arrest). The number of patients in study groups (Group 1-3) respectively as follows; 45, 26, 15. Fifty two of patients were male (60.5%) and thirty four (39.5%) of them were female and the mean age of patients was 70 ± 12 years. The mean BMI values of the three groups are summarized in Figure 1. When studied in terms of primary disease, sixty three (73%) of the cases had a diagnosis of COPD, eighteen (20%) had a diagnosis of OSAS, two (2.3%) had a diagnosis of Overlap syndrome, two (2.3%) had a diagnosis of restrictive disorder associated with kyphoscoliosis and one (1.2%) had a diagnosis of other diseases (Figure 2). Eighty percent [12] of the obese patients were female, and 20% (3) of them were male. There were more female patients in the obese group (p=0.01). The intubation ratio was found to be 31.2% in the first group, 30.3% in the second group and 40% in the third group. Although there was no statistically significant difference between the groups, the intubation ratio was higher in the third group (p=0.79).

Mortality was observed in ten patients (22.5%) in the first group, three patients (11.5%) in the second group and three patients (20%) in the third group. No statistically significant difference was found between the groups (p=0.53). The length of stay in the ICU was 10 ± 3 days in the first group, 9 ± 6 days in the second group and 10 ± 12 days in the third group. No statistically significant difference was found between the groups (p=0.93).

The length of stay in the hospital was 17 ± 13 days in the first group, 19 ± 7 days in the second group and 22 ± 11 days in the third group. No statistically significant difference was found between the groups (p=0.34).
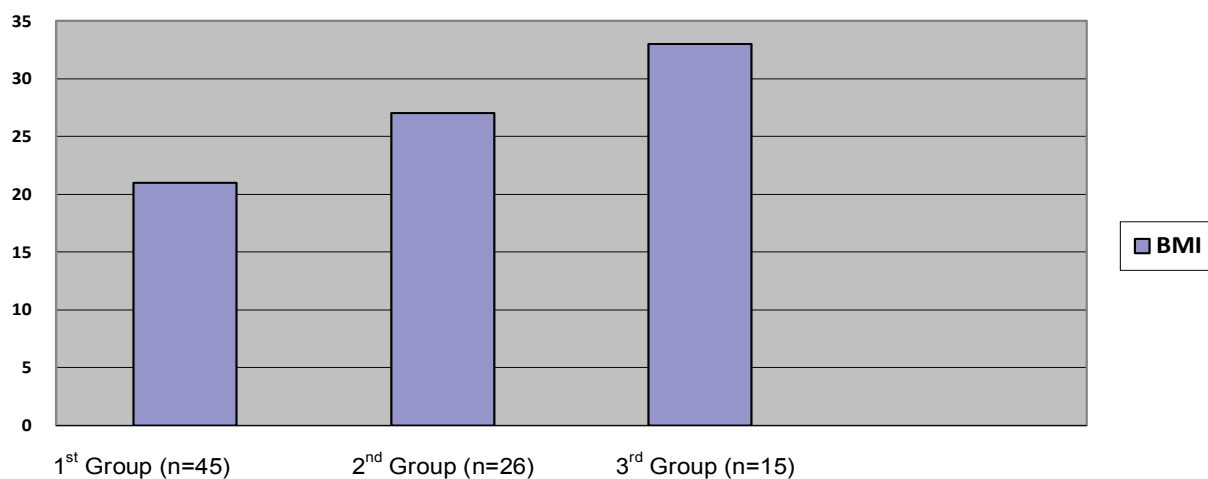
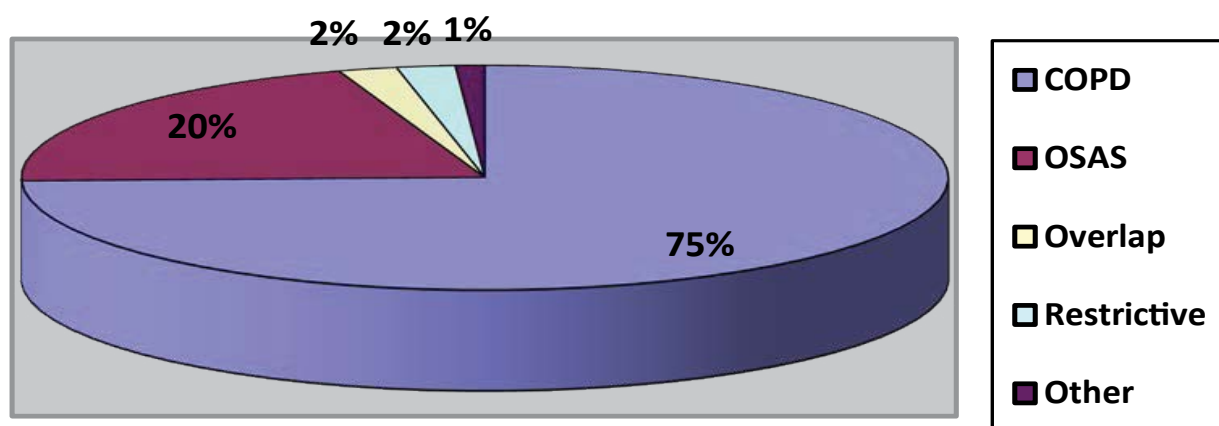**Figure 1:** Mean Body Mass Index (BMI) values

Figure 2: The distribution of the patients according to their primary diagnoses (COPD: Chronic Obstructive Pulmonary Disease; OSAS: Obstructive Sleep Apnea Sendrome)

When the success of NIMV was studied in terms of groups, it was found to be 50.2% in the first group, 28.3% in the second group and 21% in the third group. No statistically significant difference was found between the groups (p=0.79). However, the success rate of NIMV was lower in obese patients. There was pneumonia as an additional disease in 25.9% of the fifty eight patients with successful NIMV and in 44% of the twenty eight patients with unsuccessful NIMV. Although it was not statistically significant, there rate of patients with pneumonia was higher in the group with unsuccessful NIMV.

When the groups were studied, no significant difference was found in the respiratory rate before NIMV application between the groups (p=0.47). The mean respiratory rate of the first hour after NIMV application was 21 ± 4 in the first group, 20 ± 4 in the second group and 26 ± 6 in the third group. In obese patients, the respiratory rate of the first hour was higher, and this difference was statistically significant (p=0.05) (Figure 3). A total of 15.5% of the patients with successful NIMV and 21.4% of those with unsuccessful NIMV had OSAS. No statistically significant difference was found (p=0.55).

The mean serum CRP level was 7 ± 6mg/L in the first group, 9 ± 6mg/L in the second group and 6 ± 5 mg/L in the third group. There was no statistically significant difference between the groups. (p=0.64). However, while the mean CRP level was 6 ± 6mg/L in the group with successful NIMV, it was 10.1 ± 6mg/L in the group with unsuccessful NIMV. Accordingly, the CRP level was statistically higher in the group with unsuccessful NIMV (p=0.01).

The mean APACHE II score was 23.2 ± 3.9 in patients with unsuccessful NIMV, and this was significantly higher compared to patients with successful NIMV (p=0.001). When the cases in which either mortality was observed or not were investigated, the mean APACHE II score values were 23 ± 2 and 17.9 ± 4, respectively. The APACHE II values in the group in which mortality was seen was higher, and this difference was statistically significant (p=0.01).

Although the first-hour and fourth-hour values of $PaCO_2$ were higher in the obese group after NIMV application and the fourth-hour pH values were lower in this group, there was no significant difference between the three groups. However, the first-hour pH value was found to be lower in obese patients and first day and discharge $PaCO_2$ values were found to be statistically higher in these patients. (p<0.05, p=0.04, p<0.05, respectively) (Table 2).

Although the initial respiratory rates of the patients of the three groups were closer to each other, the first-hour respiratory rate after NIMV application was found to be higher in the obese group (mean= 27 ± 6 per minute, p=0.04). In terms of ventilator parameters, the mean IPAP values were 16 ± 2cm H_2O in the first group, 16 ± 3cm H_2O in the second group and 20 ± 3 cm H_2O in the third group. The NIMV pressure values were in significantly higher in the obese group (p=0.001). When the mean EPAP values were compared, they were 6 ± 1 cm H_2O in the first group, 7 ± 2cm H_2O in the second group and 9 ± 2 cm H_2O in the third group. A statistically significant correlation was found between an increase of BMI and EPAP values (p=0.001) (Table 3).

Discussion

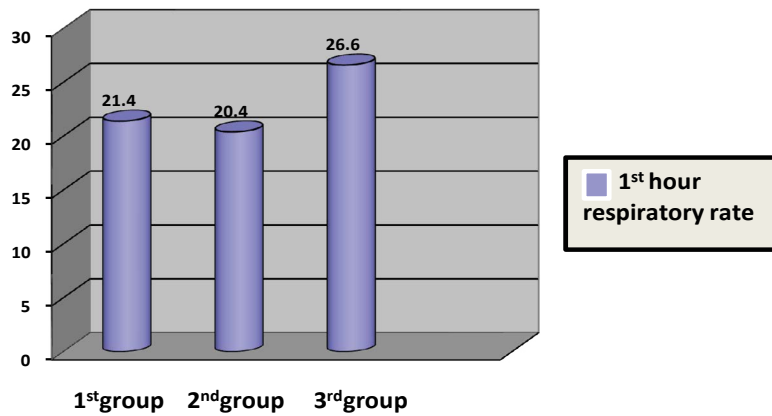In this study, NIMV application and its results resulted in

Figure 3: First-hour respiratory rates of the groups after the application of Noninvasive Mechanical Ventilation (NIMV)

Table 2: Arterial Blood Gas (ABG) values during the treatment progress.

		1st group	2nd group	3rd group	p
Initial	pH	7.27 ± 0.5	7.26 ± 0.3	7.27 ± 0.4	0.74
	PaO_2	54 ± 29	49 ± 14	62 ± 37	0.37
	$PaCO_2$	71 ± 19	73 ± 17	71 ± 15	0.93
	HCO_3	31 ± 7	30 ± 11	32 ± 6	0.89
1st hour	pH	7.32 ± 0.5	7.32 ± 0.6	7.29 ± 0.3	**0.04***
	PaO_2	60 ± 21	61 ± 19	62 ± 29	0.44
	$PaCO_2$	62 ± 16	61 ± 12	66 ± 13	0.11
	HCO_3	30 ± 7	32 ± 6	28 ± 7	0.90
4th hour	pH	7.35 ± 0.4	7.36 ± 0.6	7.31 ± 0.8	0.11
	PaO_2	65 ± 16	63 ± 17	64 ± 14	0.94
	$PaCO_2$	60 ± 13	57 ± 14	67 ± 15	0.35
	HCO_3	30 ± 6	30 ± 6	30 ± 7	0.53
24th hour	pH	7.37 ± 0.5	7.35 ± 0.7	7.35 ± 0.5	0.33
	PO_2	68 ± 21	63 ± 24	76 ± 13	**0.02***
	PCO_2	55 ± 13	56 ± 13	65 ± 18	**0.04***
	HCO_3	30 ± 6	33 ± 7	32 ± 8	0.40
Discharge	pH	7.39 ± 0.1	7.40 ± 0.6	7.38 ± 0.1	0.52
	PaO_2	66 ± 28	63 ± 16	61 ± 19	0.10
	$PaCO_2$	52 ± 25	53 ± 15	63 ± 15	**0.05***
	HCO_3	29 ± 8	32 ± 7	38 ± 9	**0.04***

* $p < 0.05$ between groups

Table 3: The differences between mean Inspiratory Positive Airway Pressure (IPAP) and Expiratory Positive Airway Pressure (EPAP) values in terms of body mass index (BMI)

	1st Group	2nd Group	3rd Group	p
Inspiratory Positive Airway Pressure (IPAP)	16 ± 2	16 ± 3	20 ± 3	**0.001***
Expiratory Positive Airway Pressure (EPAP)	6 ± 1	7 ± 2	9 ± 2	**0.001***

* $p < 0.05$ between groups.

differences in obese patients compared to the other groups. In the group of obese patients, the response in the ABG analysis to NIMV application was slower compared to other groups and the carbon dioxide ratios progressed higher in the progress of treatment. When obese patients were compensated with higher IPAP values, the IPAP and EPAP levels increased with BMI.

Obesity is occurring at an increasing rate, not only in developed countries but also in developing countries. Previous publications have indicated that OHS is one of the important causes of the respiratory failure and occurs in higher ratios in females. Among them, the obesity ratio was found to be higher in females in a study which included 219 patients and in which the influences of obesity in the ICU were studied [12]. Similarly, in a study including 2148 patients in the intensive care unit that investigated the influences of BMI, the authors found that 65% of obese patients were female [13].

In a study comprising seventy-three patients with hypercapnic respiratory failure, the authors found that the ratio of females among obese patients was 72% [14]. In a study conducted in Turkey, the obesity incidence was found to be 15% to 16% and the obesity ratio was found to be 20% in males and 40% in females [15]. In this study, 17% of the patients were obese, of which 80% were female. Obesity is seen more commonly in young adults, and the lower incidence of obesity in elderly people may be due to cardiovascular events [13]. However, in this study, the mean age was around the geriatric age group and there was no difference in age between the groups.

Goulenok and EI-Solh investigated the influence of obesity on the patients in the ICU, and their results from two distinct studies demonstrated that the mortality ratio was statistically higher in obese patients [16,17]. In a study that comprised fifty morbid obese patients, the authors found a higher mortality in the group having greater BMI [18]. In two distinct studies, the authors found no significant relationship between mortality and obesity [12,19].

In a meta-analysis comprising 88051 patients, no significant relationship was found between obesity and mortality [20]. However, because the patients were of heterogeneous groups, this study does not provide additional information concerning obese patients.

In our study, although the mortality ratios in obese patients were found to be higher, this result was not statistically significant. Previous studies investigating the effect of BMI on mortality rates in ICU patients concluded that mortality was higher in obese patients [12,17,18]. However, in these studies, the ratio of morbidly obese patients was higher than in our study.

In recent studies, the utility of the serum CRP level as an important indicator of inflammation and respiratory failure has been investigated. Additionally, various studies have showed that the level of CRP is increased in obesity. It was found that the elevation of CRP was associated with the failure of mechanical ventilation and with the length of intubation duration in a study of thirty patients in the ICU [21]. In a study of ninety-five patients, the authors found that higher APACHE II and CRP levels were related to the failure of NIMV in patients with acute hypercapnic respiratory failure [22]. In another study, the authors found that in their cohort of sixty patients with acute hypercapnic respiratory failure, APACHE II and CRP levels were independent risk factors for determining the success of treatment with NIMV [23]. In a study, it was found that higher CRP values were associated with poor prognosis in patients with OHS in which NIMV was applied. In this study, a statistically higher CRP level was found in the unsuccessful NIMV group [24].

How the presence of the accompanying pneumonia in patients with acute hypercapnic respiratory failure affects the success of NIMV is another important issue. Although the majority of the studies conducted for this purpose did not contain hypercapnic patients, some studies have demonstrated that the success rates of NIMV is lower in pneumonia patients with hypercapnic respiratory failure. In a postmortem study of forty-three patients who were hospitalized

due to COPD attack and in which early period mortality was seen, the authors identified that the most important cause of death was pneumonia [25]. In various clinical studies, it has been stated that the ratio of intubation and mortality are higher in cases experiencing pneumonia due to attacks of COPD [26]. In our study, there was pneumonia in 44% of patients in the unsuccessful NIMV group, and a higher ratio of pneumonia was noticeable in the unsuccessful group.

Concerning the obese patients, the lengths of stay in the ICU is another issue to be emphasized. Among them, in a meta-analysis comprising 62045 patients, it has been emphasized that the lengths of stay in the ICU of the patients with BMI >30 kg/m² is higher than that of the patients with BMI<30kg/m² [27]. In a study in which the influence of BMI on the length of stay in the ICU was investigated, it was reported that BMI does not affect the length of stay in the ICU, length of stay in hospital, mortality and intubation ratio [13]. In another study reporting that obesity does not affect the length of stay in the ICU, it was also found that there was no difference between obese and non-obese patients in terms of mortality and intubation [14]. In this study, there was no difference between the groups in terms of the length of stay in the ICU and the length of stay in hospital. Again, no difference was observed between the groups in terms of intubation ratios and mortality.

Alterations in ABG, particularly in pH, are an important criterion in evaluating the success of NIMV [28]. In several studies, it has been reported that patients with unsuccessful NIMV have lower pH values compared to those with successful NIMV [29]. On the other hand, no relationship has been shown between basal ABG values and between the responses to NIMV [30]. In a study involving seventy-six morbid obese patients having acute respiratory failure the authors emphasized that there was a delayed response to NIMV in more than the half of the patients and that the response in pH and $PaCO_2$ levels was not sufficient at the end of the first hour [31]. In a study, it was emphasized that more time is required for $PaCO_2$ to be reduced to below the 50mmHg level in obese patients. In a study which included forty-one obese hypercapnic patients, the authors reported that there was no difference between obese and non-obese patients in terms of carbon dioxide elimination rate [32].

Similarly, in this study, in obese patients, the first-hour pH was lower and first day- and discharge-$PaCO_2$ values were higher after NIMV application compared to the control group. Thus, we suggest that pH and $PaCO_2$ may be insufficient for the evaluation of the success of NIMV at an early period in obese patients. Furthermore, the application of failure criteria of NIMV in obese patients in the early period may lead to the earlier cessation of NIMV, which may be unnecessary and may lead to unnecessary intubations. Similarly, it is known whether the improvement in respiratory rate within the first hour is important in the evaluation of the objective response to NIMV [33-35]. In this study, the respiratory rate at the end of the first hour after NIMV application was found to be higher in obese group, compared to other groups.

The limitations of the study are as follows: this was a retrospective study and the number of the patients who were included to the study, especially morbidly obese ones, was limited. Further larger prospective studies are necessary to clarify the effects of BMI on NIMV application.

Conclusion

In conclusion, there are differences in the evaluation of the early response in obese patients with acute hypercapnic respiratory failure in whom NIMV has been applied compared to patients with normal BMI. In NIMV application, the first-hour respiratory rates of obese patients, and their first-hour- carbon dioxide values and their carbon dioxide values during the transfer from the intensive care unit progress at higher levels. It should be taken into account that the early response can be later than the normal response in obese patients in whom NIMV is applied due to acute hypercapnic respiratory failure.

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