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NT-proBNP levels during spontaneous breathing test and its association with successful weaning in patients undergoing mechanical ventilation in the intensive care unit

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Abstract

Introduction: Weaning of the patient is one of the important medical challenges. One of the most important causes of failure in weaning is cardiovascular disorder. *NT-proBNP* (N-terminal portion of proBNP) is a specific serum marker for cardiac dysfunction. This study was conducted to evaluate the level of NT-proBNP during the spontaneous breathing test (SBT) in patients undergoing mechanical ventilation in the intensive care unit (ICU) and its association with successful weaning.

Methods: In this cross-sectional study, we enrolled 42 intubated patients who were admitted to the ICU ward of Imam Reza hospital and were clinically weaned in 2017. After obtaining informed consent, SBT was started for the patient. One and half hours after SBT onset, a venous blood sample was obtained, the patients were followed for SBT test success, and the results were recorded. Patients were extubated in stabilized condition or continued mechanical ventilation if needed. Finally, the data were analyzed with SPSS v. 16.0 software.

Results: SBT was successful in 45.2% of patients. Of all the patients, 54.8% were male. The most common cause of hospitalization was chronic obstructive pulmonary disease (COPD) (35.7%). The mean age of patients with successful SBT was 67.53 ± 6.14 years, and in patients with unsuccessful SBT was 68.70 ± 5.44 years. There was a significant difference between NT-proBNP levels half an hour after SBT between the two groups of patients with successful (7.15 ± 31.18) and unsuccessful (59.61 ± 196.51) SBT. NT-ProBNP changes before and half an hour after SBT in both groups were statistically significant.

Conclusion: NT-ProBNP is a predictor criterion of success in weaning of the patients, and as the level of NT-proBNP increases, the rate of failure in weaning increases.

Introduction

Extubating of the patients from the ventilator (weaning) is always challenging for clinicians because recognition of the adequate time of weaning is complicated and difficult.[1] In most of the patients, the weaning from mechanical ventilation is successful, but, in one-third of the cases, the weaning process fails.[2] Spontaneous breathing test (SBT) is the most accurate index to predict weaning success. However, 75%-80% of successful SBTs have had successful weaning.[3] Cardiovascular dysfunction may lead to weaning failure.[4-6] Diagnosis of left heart failure in intubated patients is a challenging, expensive and invasive process.[5,7,8] NT-proBNP (N-terminal portion of proBNP) is a sensitive and specific serum marker for cardiovascular dysfunction,[9-11] and could be useful in the diagnosis of heart failure, as much as BNP.[12] Recent studies have shown that increased (NT-proBNP) level during SBT may indicate cardiac complications leading to weaning failure rather than pulmonary complications.[13] Considering the importance of the subject and the different results of previous studies, this study aimed to investigate the association of NT-proBNP level during SBT in patients undergoing mechanical ventilation in the intensive care unit (ICU) with successful weaning.

Methods

In this cross-sectional study, 42 intubated patients (according to the Cochran formula for determining the

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appropriate sample size) of the ICU of Imam Reza hospital of Tabriz city, who had indications to wean from the ventilator machine, were gathered using simple random sampling and enrolled in the study. After obtaining informed consent from patients' companions, the SBT trial was started. Inclusion criteria included consciousness and stable hemodynamic status on no vasopressor, positive end-expiratory pressure <8, respiratory rate <35, tidal volume (TV) > 5 mL/kg, PaO2 >60, SaO2 >90%, FiO$_2$ <40, effective cough, without significant respiratory acidosis and controlled metabolic disorders. Exclusion criteria included cardiac arrest with neurologic sequels, renal failure with glomerular filtration rate (GFR) < 30 mL/min or more than 25% increase in serum creatinine in the last 24 hours, pregnancy and breastfeeding, tracheostomy, myasthenia gravis or acute polyclonal neuropathy, chronic end-stage diseases, and heart failure.

Prior to the trial, 2 mL blood sample was taken into a tube containing EDTA and aprotinin and centrifuged at 4 degrees for 4 minutes. Isolated plasma was collected in an Eppendorf tube and stored at -80°C. Half an hour after SBT initiation, another blood sample was obtained and prepared in the mentioned conditions. Samples were stored at -80°C until the end of sampling, and NT-proBNP level was measured by BNP-32 kit (ESA). Meanwhile, the patients were evaluated for the success of the SBT trial, and the results were recorded. Patients were extubated in stabilized condition or continued on mechanical ventilation. Weaning failure interpreted as the failure in the SBT trial or the need for re-intubation during the next 48 hours of extubation

Data and Statistical Analysis
Data were analyzed using SPSS for Windows, version 16.0. (Chicago, SPSS Inc; 2007). For descriptive statistical evaluation of the study population, mean ± SD, frequency, and percentage of frequency were reported. For statistical analysis of the variables, independent t test and chi-square tests were used for data with normal distribution, and non-parametric test for abnormal distribution. P values less than 0.05 were considered statistically significant.

Results
In this study, 19 (45.2%) of the 42 patients, had successful extubation. The results of the Kolmogorov-Smirnov test showed that except the NT-proBNP level, all variables had a normal distribution. Table 1 shows the demographic and baseline characteristics of patients based on the variables of the study.

The average of NT-proBNP level before and during SBT is reported in Table 2. Results of t test showed that there was a significant difference between NT-proBNP changes before and during SBT ($P = 0.001$).

The main objective of this study was to determine the relationship between NT-proBNP level before and during SBT with the rate of success in SBT and weaning. The result of the independent t test showed that NT-proBNP level before SBT was not statistically meaningful. However, there were significant differences in NT-proBNP level during SBT between two groups of patients with successful and unsuccessful SBT (Table 3).

Discussion
In the present study, we studied the predictive value of NT-proBNP level during SBT with successful weaning of mechanical ventilation in ICU patients. In this study, 45.2% of all patients had successful SBT. There was a significant difference between NT-proBNP level before and half an hour after SBT in two groups of patients with successful and unsuccessful weaning. There was

Table 1. Demographic and baseline characteristics of patients based on variables

Variable	Successful mechanical weaning (n = 19)	Unsuccessful mechanical weaning (n = 23)	P value
Age (y)	67.53 ± 6.14	68.70 ± 5.44	>0.05 (NS)
Gender, male, n, (%)	8 (42)	15 (65)	>0.05 (NS)
Body mass index (mean ± SD)	23.95 ± 2.46	22.61 ± 3.54	>0.05 (NS)
Mechanical ventilation duration (day) (mean ± SD)	7.68 ± 2.67	8.83 ± 2.74	>0.05 (NS)
Systolic blood pressure (mean ± SD)	116.84 ± 12.50	123.04 ± 17.17	>0.05 (NS)
Diastolic blood pressure (mean ± SD)	75.53 ± 5.50	78.9 ± 7.22	>0.05 (NS)

Abbreviations: NS: Not significant, SD: standard deviation
P value was reported based on chi-square test and independent sample t test.

Table 2. NT-proBNP levels before and during SBT in the patients

	NT-ProBNP		P value
	Pre SBT	**During SBT**	
Mean ± SD	4.84 ± 28.07	94.28121.86 ±	0.001

Abbreviation: SD, standard deviation
P value was reported based on independent sample t test.

Table 3. Comparison of NT-proBNP levels before and during SBT in patients

Variable	Measuring time	Group	Mean ± SD	P value
NT-proBNP	Pre SBT	Successful	26.69 ± 5.43	0.093
		Unsuccessful	4.08 ± 29.22	
	During SBT	Successful	7.15 ± 31.18	0.001
		Unsuccessful	59.61 ± 196.51	

Abbreviation: SD, standard deviation
P value was reported based on Independent sample t test.

not any significant relationship between the level of NT-proBNP and other variables including age, sex, body mass index, cause of hospitalization, duration of ventilation and blood pressure. El Maraghi et al's study aimed to investigate changes in BNP levels during the SBT (before and two hours later) with the result of weaning on 40 patients which showed that patients with successful weaning had a significantly lower BNP level than patients with unsuccessful weaning, and the changes in BNP level during SBT can be used as a prognostic factor for weaning success which is consistent with the results of our study.[14] In the mentioned study, the rate of success in SBT was 80% which was significantly higher than our study (45.2%). This may be due to differences in the timing of the test or gender differences leading causes of mechanical ventilation need in two studies. Also, there was no statistically significant difference between age and gender and cause of hospitalization with BNP, which was similar to our study.

Chien et al's study on patients with acute respiratory failure showed that BNP levels after 2 hours of SBT were lower in patients who had successful weaning, which is in line with the results of our study.[15] This study showed that patients who needed reintubation after successful extubation had higher levels of BNP in their blood. The high level of BNP in unsuccessful extubation was consistent with the results of the present study.

A study by Ma et al evaluated the relationship between NT-ProBNP level and weaning outcomes and its ability to predict the rate of success in weaning in cancer patients with pulmonary complications. The study showed that NT-ProBNP level is significantly high in patients who had unsuccessful weaning, which is consistent with results of our study.[16]

A study by Ouanes-Besbes et al investigated the role of NT-proBNP and plasma protein, hematocrit and fluid balance on the outcome of SBT and extubation which showed that patients who developed respiratory symptoms following the extubation had higher levels of NT-proBNP, and only this peptide could predict the post-extubation distress or intubation failure.[17] The findings of this study were similar to ours. The study by Grasso et al pointed to the usefulness of serial measurement of NT-proBNP in the diagnosis of acute cardiac dysfunction in chronic obstructive pulmonary disease (COPD) patients who were complicated to wean, which is consistent with the results of the present study.[18]

In contrast with the findings of our study, in a study conducted by Mekontso-Dessap et al there was no significant correlation between the level of BNP, one hour after SBT in patients with successful and unsuccessful weaning.[19] However, their findings suggest that BNP levels are associated with failure in weaning and long duration of weaning. One of the reasons for these differences can be related to the different blood sampling time after SBT in different studies. A study by Kanda et al and also a study by Hogenhuis et al showed that the BNP level increases with age.[20,21] These findings were reported in both healthy subjects and those with heart failure.

On the other hand, the study of Kanda et al showed that BNP levels in women 25% to 50% higher than men, which are inconsistent with the results of our study.[20] Also, the findings of a study by Principi et al, evaluating the ICU patients, highlighted the effect of age on the NT-proBNP level.[22] In overall, these findings were contrary to the findings of our study, which found no association between NT-proBNP level and gender or age. However, the studies by El Maraghi et al and Chien et al, which were on the evaluation of patients with acute respiratory failure, did not find any significant association between age and gender with the levels of BNP.[14,15] The results of the mentioned studies were consistent with the findings of our study.

Conclusion

Based on the results of this study, we could consider the NT-proBNP as a predictor of weaning success in intubated patients as an increased level of NT-proBNP indicates a higher rate of failure in weaning. Large clinical trials are recommended to confirm the NT-proBNP assay for routine evaluation weaning failure rate.

Study Highlights

What is current knowledge?
- Weaning of the patient is one of the important medical challenges.
- One of the most important causes of failure in weaning is cardiovascular disorders.
- NT-Pro-BNP is a specific serum marker for cardiac dysfunction.

What is new here?
- NT-ProBNP is a predictor criteria of success in weaning in patients and as the level of NT-Pro-BNP increases, the rate of failure in weaning increases.

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