

PLASMA B-TYPE NATRIURETIC PEPTIDE AS A PREDICTOR OF WEANING
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ABSTRACT

Background: There are different criterias and tools act as predictors of weaning outcome of the patients under mechanical ventilation. But each of them has variable predictability. About 20% to 30% of patients who meet the certain criterias for weaning initially, ultimately fail to wean from mechanical ventilation. Cardiovascular dysfunction could be a major underlying mechanism of weaning failure. Recent data suggest that plasma B-type natriuretic peptide, a marker for cardiovascular dysfunction, may predict the outcome of weaning from mechanical ventilation. **Objective:** The purpose of the study was to evaluate the role of plasma B-type natriuretic peptide as a predictor of weaning among the patients under mechanical ventilation in ICU. **Methodology:** This study was a prospective cohort study. This study was conducted in the Department of Anesthesia, Analgesia and Intensive Care Medicine at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh over a period of 2 years. Study population was selected for weaning from mechanical ventilation support for the first time in the age group of more than 18 years with both sexes. Patients with pre-existing diseases that elevate the plasma BNP level were excluded from the study. Weaning criteria was selected by ICU consultant following the standard ICU protocol for every patients enrolled in this study. Patients were subdivided into weaning success and weaning failure groups according to the outcome of weaning process. Plasma BNP level of all patients was measured before and after 2 hours of spontaneous breathing trial. Each blood sample (3ml) was collected by ICU lab technician into a vacutainer with EDTA for anticoagulation. Blood samples were sent to the biochemistry lab and analysis was done by chemiluminescent microparticle immunoassay (CMIA). Serial arterial blood gases done within ICU lab before and after 2 hours of SBT and 12 hourly up to 48 hours. Patients who were extubated would be followed up for 48 hours after SBT. **Result:** A total number of 30 patients were recruited for this study. One-third (33.3%) of the patients failed on SBT. The mean age of weaning success and failure groups were 54.90±9.787 years and 57.60±10.091 years respectively. The mean percent changes of BNP (pg/ml) during 2-h of SBT in weaning success and failure groups were 38.41±9.379 and 59.51±2.940 respectively, the difference was statistically significant (p=0.01). The receiver-operating characteristic curve (ROC) analysis for BNP as a predictor of weaning outcome, showed that the area under the curve (AUC) was 0.89. It was found that change of BNP level < 42.5% from baseline had the best combination of sensitivity (90%) and specificity (80%) in predicting weaning outcome. **Conclusion:** Plasma BNP level can be used as a predictor of weaning outcome among the patients under mechanical ventilation.

KEYWORD: Plasma BNP, Anesthesia, Analgesia, Intensive Care.**INTRODUCTION**

Weaning is the term frequently used to describe the gradual reduction of ventilatory support from a patient whose pulmonary and other conditions are improving.^[1] Delayed weaning from ventilatory support expose patients to unnecessary complications.^[2] Patients should therefore be weaned from mechanical ventilation as quickly as possible. The ventilator discontinuation process is a critical component of ICU care and also very

challenging for clinicians.^[2] Furthermore, both delayed and premature weaning may be harmful as well. Weaning a patient from mechanical ventilation is an art and very unpredictable as well. The current parameter used to predict successful weaning which is American College of Chest Physician (ACCP) and Association of Respiratory Care (AARC) Respir care (2002) have shown variable predictive value. About 75% of patients who meet specific criteria can tolerate spontaneous

breathing trial (SBT) and the rest of the patients fail to tolerate SBT. On the other hand, 30% of patients who never satisfy weaning criteria can be weaned from ventilator.^[3] That is why, weaning criterias and tools should be more precised to predict the outcome of weaning accurately.

BNP is secreted by ventricular cardiomyocytes in response to myocardial stretch by volume or pressure overload. During two hours of SBT which is currently the most accurate index for predicting the weaning success, there is an increase of in cardiac preload and afterload of the both side of heart caused by intrathoracic pressure shift, increase catecholamine secretion and work of breathing.^[5] This increased volume and pressure shifting precipitate weaning induced cardiac dysfunctions like weaning induced pulmonary oedema (WiPO) and weaning induced cardiac ischemia.^[6] Though both of them contribute weaning failure, impact of WiPO is more significant. An increase of plasma BNP during SBT, can demonstrate these cardiac dysfunctions.

BNP is the most reliable hormonal marker for left ventricular dysfunction and its plasma levels correlate closely with indices of systolic function in patients with stable and decompensated heart failure.^[7] Therefore, BNP is currently a good predictor of different cardiac diseases. However, during weaning of mechanically ventilated patients, role of plasma BNP level as a predictor of successful weaning outcomes is to be evaluated.

Current evidence on the predictive ability of BNP on weaning failure has been uncertain, and has not been integrated into clinical practice guideline. This present study was undertaken to evaluate the plasma level of B-type natriuretic peptide (BNP) as a predictor of weaning outcome among the patients under mechanical ventilation.

OBJECTIVE

General Objective

- To evaluate the level of plasma B-type natriuretic peptide (BNP) as a predictor of weaning outcome before and after 2 hours of spontaneous breathing trial (SBT).

Specific Objectives

- To measure the serum level of BNP before and after 2hours of spontaneous breathing trial (SBT) among patients under mechanical ventilation.
- To compare the serum level of BNP between weaning successful and weaning failed patients.

MATERIAL AND METHODS

Study Design and settings

This study was a prospective cohort study. This study was carried out from July 2018 to June 2020 for a period of two (02) years. Data was taken after the approval of

Institutional Review Board (IRB) up to June 2020. This study was conducted in the Department of Anaesthesia, Analgesia and Intensive Care Medicine at Bangabandhu Sheikh Mujib Medical University, Dhaka, Bangladesh. Patients who were considered for liberation from mechanical ventilation support for the first time in the age group of more than 18 years with both sexes were selected as the study population. Patients with pre-existing diseases that elevate the plasma BNP level were excluded from the study. Weaning criteria was selected by ICU consultant following the standard ICU protocol for every patient enrolled in this study. Patients were subdivided into weaning success and weaning failure groups according to the outcome of weaning process.

Sampling Technique

This study population was selected by purposive sampling technique.

Sample size

Sample size determination depends on time and resources. Therefore, it was considered that the total sample size was 30 patients. According to the weaning outcome these patients would be designed a Group A (Weaning success group) and Group B (Weaning failure group).

Selection Criteria

• Inclusion Criteria

- All patients who were intubated and had shown improvement or resolution of the underlying cause of respiratory failure.
- Sedation stopped during the previous 48 hours and analgesia might continued.
- Patients age more 18 years.
- Patients of both sexes.
- Patients whose relatives give written inform consent.

• Exclusion Criteria

- Patients with heart failure (right or left), pulmonary hypertension, valvular heart diseases and atrial fibrillation.
- Patients having Acute (creatinine>350mmol/l) or Chronic renal diseases under Renal Replacement Therapy (RRT).
- Patients with cirrhosis of liver.
- Patients with tracheostomy.
- Patients with hyperthyroidism as this condition may be associated with increased BNP level.
- Prolonged cardiac arrest with poor neurological prognosis.
- Patients having no written inform consent.

Study Procedure

Patients admitted in the ICU were enrolled for this study after the exclusion of the previously diagnosed diseases that elevate the plasma BNP level. Patient details like age, sex, address was documented in the case record form (CRF) supplied. The informed written consent was taken from patient's relatives. Detailed history and clinical examination findings were documented in case

record form (CRF). Initial mortality prediction was done by APACHE-2 (Acute physiology and Chronic Health Evaluation) and qSOFA (quick Sequential Organ Failure Assessment). All previous investigations done for these patients were recorded in the investigation record form in ICU. Relevant investigations for this study like BNP and ABG were recorded in the case record form (CFR).

Data Collection

The study was done in ICU of BSMMU. Patients during the study period were selected if they fulfilled the inclusion criteria. The relevant information was recorded in the data collection sheet. The data collection was done by the researcher himself.

Statistical Analysis

Statistical analysis was performed by Windows based software named as Statistical Package for Social Science (SPSS), versions 22.0 (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp).

Continuous data that were normally distributed were summarized in terms of the mean, standard deviation, median, minimum, maximum and number of observations. Categorical data were summarized in terms of frequency counts and percentages. For end points analysis, Chi-square test was used for categorical data and Student t Test for continuous data.

RESULTS

A total number of 30 patients were recruited for this study. Of the 30 patients included in the study 20(67.7%) patients were in the weaning success group designated as Group A and the rest 10(33.3%) patients were in the weaning failure group designated as Group B. The plasma BNP level was measured in all patients before and after 2-h of SBT, which was significantly higher in weaning failure group than weaning success group ($p=0.01$), the mean percentage change of BNP in during 2-h of SBT was evaluated by ROC curve.

Table 1: Age Distribution of Study Population. Group-A (Weaning success) and Group-B (Weaning failure) (N=30).

Age Group	Weaning Group		Total	P value
	Group-A	Group-B		
32 to 40 Years	2(10.0%)	1(10.0%)	3(10.0%)	0.49*
40 to 60 Years	14(70.0%)	5(50.0%)	19(63.3%)	
60 to 72 Years	4(20.0%)	4(40.0%)	8(26.7%)	
Mean±SD	54.90±9.787	57.60±10.091	55.80±9.79	0.48**

Range: 32 to 72 years; *Chi-square test was performed to see the level of significance; ** P value was calculated by unpaired t test to see the level of significance.

Table 1 showed the age distribution of study population. In weaning success group, the most common age group was 40 to 60 years which was 14(70.0%) cases followed by 60 to 72 years and 32 to 40 years age group which was 4(20.0%) cases and 2(10.0%) cases respectively. In weaning failure group, the most common age group was 40 to 60 years which was 5(50.0%) cases followed by 60 to 72 years and 32 to 40 years age group which was

4(40.0%) cases and 1(10.0%) case respectively. The mean age with SD of weaning success and failure group were 54.90±9.78 years and 57.60±10.09 years respectively. The age range of study population was 32 to 72 years. The difference of age group of weaning success and failure groups were not statistically significant (p value=0.48).

Table 2: Gender Distribution of Study Population. Group-A (Weaning success) and Group-B (Weaning failure) (N=30).

Gender	Weaning Group		Total	P value
	Group-A	Group-B		
Male	18(90.0%)	4(40.0%)	22(73.3%)	0.004
Female	2(10.0%)	6(60.0%)	8(26.7%)	
Total	20(100.0%)	10(100.0%)	30(100.0%)	

Male: Female=2.75:1; Chi-square test was performed to see the level of significance.

Table 2 showed the distribution of study population according to gender. In this study male was predominant in number than female which was 22(73.3%) cases and 8(26.7%) cases respectively. Among 20 cases of weaning success group male was more than female which was 18(90.0%) cases and 2(10.0%) cases respectively. In 10 cases of weaning failure group female was more than male which was 6(60.0%) cases and 4(40.0%) cases respectively. The male and female difference between weaning success and failure groups was statistically

significant (p value=0.004). The ratio between male and female was 2.75:1.

Table 3: BNP level (pg/ml) in Gender Distribution of Study Population. Group-A (Weaning success) and Group-B (Weaning failure) (N=30).

BNP Value	Gender	Mean±SD	P value
Before SBT	Male	44.97±20.40	0.001
	Female	67.70±22.25	
After 2-h of SBT	Male	146.51±130.28	0.007
	Female	302.60±130.67	

SBT- Spontaneous breathing trail. P value was calculated by unpaired t test to see the level of significance.

Table 3 shows the distribution of study population according to gender. Before SBT, the mean with standard deviation of BNP in male and female was 44.97±20.402 and 67.70±22.254 respectively. The difference of BNP value of male and female before SBT was statistically significant (p=0.001). After SBT, the mean with standard deviation of BNP in male and female was 146.51±130.28 and 302.60±130.679 respectively. The difference of BNP value of male and female after SBT was statistically significant (p=0.007).

Table 4: Chronic Co-Morbidities of Study Population. Group-A (Weaning success) and Group-B (Weaning failure) (N=30).

Chronic Co-Morbidities	Weaning Group		Total	P value
	Group-A	Group-B		
COPD+HTN+DM	1(5.0%)	0(0.0%)	1(3.3%)	0.20
DM	5(25.0%)	1(10.0%)	6(20.0%)	
DM+HTN	7(35.0%)	8(80.0%)	15(50.0%)	
DM+IHD	2(10.0%)	0(0.0%)	2(6.7%)	
HTN	1(5.0%)	1(10.0%)	2(6.7%)	
HTN+IHD	4(20.0%)	0(0.0%)	4(13.3%)	
Total	20(100.0%)	10(100.0%)	30(100.0%)	

COPD= Chronic Obstructive Pulmonary disease; HTN=Hypertension; DM=Diabetes mellitus; IHD=Ischemic heart disease; Chi-square test was performed to see the level of significance.

Table 4 showed the chronic co-morbidities of study population. In weaning success group most, common co-morbidity was diabetes mellitus with hypertension which was 7(35.0%) cases followed by diabetes mellitus, hypertension with ischemic heart disease and diabetes mellitus with ischemic heart disease which were 5(25.0%) cases, 4(20.0%) cases and 2(10.0%) cases respectively. In weaning failure group diabetes mellitus with hypertension was the most common which was 8(80.0%) cases. The difference of chronic co-morbidities between weaning success and failure groups was not statistically significant (p value=0.20).

Table 7: The mean percent change in plasma BNP level (pg/ml) during 2-hours of SBT. (N=30).

Weaning Group	Mean±SD	P value
Success Group	38.41±9.379	0.01
Failure Group	59.51±2.940	

P value was calculated by unpaired t test to see the level of significance.

Table 6 showed the mean percent change in plasma BNP level during 2-hours of SBT. The mean percent changes of BNP with standard deviation of weaning success and failure groups were 38.41±9.379 and 59.51±2.940 respectively. The difference of changes of BNP between these two groups were statistically significant (p=0.01).

DISCUSSION

A total number of 30 patients were recruited for this study after fulfilling the inclusion and exclusion criteria. According to the outcome of SBT they were subdivided into two groups, weaning success (n=20) and weaning failure group (n=10). Regarding age distribution in

weaning success group and weaning failure group the most common age group was 40 to 60 years. The difference of age group of weaning success and failure groups were not statistically significant (p=0.49). From this finding it is very clear that the mean age of the patients in weaning success and failure groups were more or less equivalent (p=0.48). Therefore, the result is not bias based on the age of the patients. The similar age distribution is also reported by Mekontso-Dessap et al (2006) and have stated that the age group are 57 years which is consistent with the present study.^[8] Chien et al (2008) have performed a study and have found that most of the patients are in this age group under mechanical ventilation which is similar to this present study.^[9]

According to the gender distribution, this study showed male was predominant in number than female but weaning failure was more common in female patients. The male and female difference between weaning success and failure groups were statistically significant (p=0.004). The ratio between male and female was 2.75:1. Similar to this present study, Chien et al (2008) have reported that male patients are more commonly under mechanical ventilation.^[9] In this present study male was double than female. In another study Zapata et al (2011) have reported a predominance of male over female which is consistent with the present study.^[10] In this study female were more prone to weaning failure than male, which is supported by the study Ghilani et al (2020). The study demonstrates that female gender (0.401 [0.216-0.745]; p=0.004) LTC-MP (3.017 [1.027–8.862]; p= 0.046) is independent risk factor for an unsuccessful SBT.

The mean BNP values among male and female were recorded in this study and found that the mean BNP values were higher in female than male both before and after SBT, which was statistically significant ($p=0.001$). Redfield et al. (2002) mentioned that BNP level is higher in females compared to males in all age groups. The exact reason for this is still under investigation but may have to do with either the impact of estrogen, with the high estrogen levels causing higher BNP levels or the role of testosterone on lowering the level of BNP.^[11] The study finding is similar to the study finding of Redfield et al. (2002) in which BNP level is 32 % higher in female than male (CI=15% to 51%, $p < 0.001$) by Shionogi assay and 80% higher by Bisite assay (CI=50% to 116%, $p < 0.001$).

The chronic co-morbidities of study population were observed in this study. Diabetes mellitus with hypertension was the most common co-morbidity which was 15(50.0%) cases among weaning failure and success groups. The difference of chronic co-morbidities between weaning success and failure groups was not statistically significant (p value=0.206). The most common co-morbidities among the all age groups (<65year to ≥ 65 years) are hypertension (18.5%, 89.7%), ischemic heart disease (7.5%, 75.1%) and diabetes mellitus (4.3%, 33%) (Schellevis et al.1993), which is similar with this present study. Level of BNP can be elevated by hypertension in the presence of left ventricular hypertrophy.^[12] In this study both groups had hypertension as their common co-morbidity so there is no chance of bias in result regarding hypertension. Controlled diabetes mellitus has no impact over BNP level but it can be altered in the presence of Chronic heart diseases, which is consistent with this study finding.^[14]

The mean percent change in plasma BNP level during 2-hours after SBT has been recorded, which was (38.41 \pm 9.379) and (59.51 \pm 2.940) between weaning success and failure groups respectively. The difference of changes of BNP between these two groups were statistically significant ($p=0.01$). In this present study, BNP level is significantly changed at the beginning and at the end of the SBT. A study by Vieillard-Baron et al (2001) have reported that the baseline BNP levels are significantly higher in patients with cardiac dysfunction and increased significantly at the end of the T-piece trial which is consistent with the present study result.^[15] Lara et al (2013) have reported that the baseline plasma BNP level is significantly correlated to duration of weaning which is consistent with the present study.

CONCLUSION

Plasma BNP level was increased both in weaning success and weaning failure group during SBT. But it was significantly increased in weaning failure group which was evaluated by ROC curve. So, plasma BNP level can be used to predict the weaning outcome of mechanically ventilated patients.

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