Original Article

Relationship Between Brain Natriuretic Peptide and Weaning from Mechanical Ventilation and ICU Stay After Pediatric Cardiac Surgery

Ziae Totonchi[1], MD; Mohammad Mahdavi[1*], MD; Rasoul Azarfarin[2],MD; Reza Abbaszadeh[1], MD; Akbar Nikpajouh[1], PhD; Farideh Mohammadi Alasti[1], MD; Louise Jafari[1], MD; Zahra Sadat Koleini[1], MD; Elham Mohebbi[1], MD

ABSTRACT

Background: Failing heart has been described as the main mechanism of an unsuccessful separation from the mechanical ventilator after cardiac surgery. Brain natriuretic peptide (BNP) is a specific marker for cardiac dysfunction. We aimed to evaluate the relationships between BNP levels and the duration of mechanical ventilation and the length of stay at the intensive care unit (ICU) after pediatric cardiac surgery.

Methods: In this observational study, 52 infants aged between 2 and 50 months who underwent cardiac surgery were enrolled. Anesthesia and cardiopulmonary bypass methods were similar, and the weaning protocol in the ICU was the same in all the patients. The levels of pro-BNP and plasma lactate were recorded before surgery; at the time of ICU admission; and 24, 48, and 72 hours afterward. At the end of the study, the relationships between the levels of BNP and plasma lactate and the duration of mechanical ventilation and the length of stay at the ICU were assessed.

Results: Of the 52 patients, 35 (67.3%) were male. The mean age and weight were 17.14±12.50 months and 9.01±2.98 kg, respectively. The mean duration of cardiopulmonary bypass was 191.25±34.15 minutes, and the mean aortic cross-clamp time was 75.48±31.88 minutes. The mean duration of mechanical ventilation was 21.78±18.78 minutes, and the mean length of stay at the ICU was 133.67±97.68 hours. The results showed that there was no significant relationship between the pro-BNP level and the duration of mechanical ventilation ($P>0.05$). The levels of pro-BNP at the time of ICU admission and 24 and 48 hours after surgery had a direct relationship with the duration of ICU stay ($P<0.05$).

Conclusions: In the present study, higher serum pro-BNP levels at the time of ICU admission and 24 and 48 hours after admission were related to a prolonged ICU stay. However, the serum BNP level was not correlated with the duration of mechanical ventilation after pediatric cardiac surgery. ***(Iranian Heart Journal 2018; 19(4): 40-46)***

KEYWORDS: Brain natriuretic peptide, Pediatric cardiac surgery, Mechanical ventilation, Intensive care unit

[1] Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.
[2] Echocardiography Research Center, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Tehran, IR Iran.

***Corresponding Author:** Mohamad Mahdavi, MD; Associate Professor of Pediatric Cardiology, Department of Cardiac Cardiology, Rajaie Cardiovascular, Medical, and Research Center, Iran University of Medical Sciences, Vali-E-Asr Ave, Tehran, IR Iran.
Email: md_niaki@yahoo.com **Tel:** 02123922015

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Congenital heart diseases are the most common type of congenital disorders with an incidence rate of approximately 9 per 1000 live births.[1] Surgical intervention requires cardiopulmonary bypass (CPB) for myocardial protection during surgery and mechanical ventilation after CPB to maintain the oxygen supply. [2,3] CPB causes reperfusion injury recognized by the enhanced inflammatory response and systemic hyperlactatemia.[3-5] Mechanical ventilation has some side effects such as decreased cardiac output, neurological dysfunction, and hepatic and renal function impairment, all of which are correlated directly with the duration of postoperative mechanical ventilation.[6,7] Therefore, having a molecular marker to predict the postoperative complications confers an appropriate and timely management of these complications.

One of the markers investigated in this regard is brain natriuretic peptide (BNP), a 32-amino acid polypeptide hormone with diuretic, natriuretic, and vasoactive properties. A hormone produced in the atrium and ventricle in response to myositis proliferation, BNP has a unique clinical application and is used as a biomarker for the management of adult and childhood heart diseases.[8,9] This hormone is released in response to volumetric overload and increases the elongation of the ventricular wall and is released into the circulatory system.[10,11] Active and inactive forms of BNP are stored in myocytes.[12] BNP has been studied in children and adults who need mechanical heart support.[13] Recent studies have suggested that the level of BNP before separating the device can independently predict the probability of failure in separation from the ventilator.[14-17] Clinically, BNP levels are widely used in patients with heart failure to identify and classify the risk as a predictor of outcomes such as readmission and mortality.[18-21] An increased level of pro-BNP is considered to be a biomarker of ventricular dysfunction and can detect early decompensated heart failure after cardiac surgery.[18-21] High postoperative pro-BNP levels in post-cardiac surgery patients are associated with an increase in hospitalization duration and mortality.[22] Since previous studies have suggested that the pro-BNP level may offer a robust marker for the prognosis of weaning from the ventilator in CPB and the length of stay at the intensive care unit (ICU) and the hospital in different settings independently. Given the importance of the prognosis of mechanical ventilation and other clinical postoperative outcomes following cardiac surgery in children, we aimed to investigate the predictive power of the BNP level in separation from mechanical ventilation, the length of ICU stay, and the duration of hospitalization after pediatric cardiac surgery.

METHODS

Patients and Study Design

This prospective observational study recruited 52 infants aged between 2 and 50 months who underwent cardiac surgery in a university hospital. The levels of pro-BNP and plasma lactate were recorded before surgery; during ICU admission; and 24, 48, and 72 hours afterward. At the end of the study, the relationships between the levels of BNP and plasma lactate and the duration of mechanical ventilation and the length of stay at the ICU were assessed. The methods of anesthesia and CPB were similar, and the weaning protocol in the ICU was the same in all the patients. At the end of the study, the relationships between the levels of pro-BNP and plasma lactate and the duration of mechanical ventilation and the length of ICU stay were evaluated in the study population.

The patients were divided into 2 subgroups according to their time of weaning from the ventilator: the extubation time less than 12 hours after surgery and the extubation time at least 12 hours after surgery. Then, the groups were compared in terms of demographic data and the other outcome measures such as the duration of CPB, the duration of the operation,

the aortic cross-clamp time, the length of ICU stay, and the levels of serum pro-BNP and serum lactate.

Statistical Analysis

The data analyses were performed using the SPSS software, version 20 (IBM Statistics, New York, USA). To describe the characteristics of the research units in both groups, we used descriptive statistics—including central inclination and dispersion indices, means ± standard deviations (SDs) when the data were normally distributed, medians (Q1–Q3) when the distribution was not normal, and frequency distributions—for the nominal or categorical data. To test the correlation between 2 variables, we applied the Pearson correlation test in the case of a normal distribution and the Spearman correlation in the case of data deviation from the normal distribution. The independent-samples *t*-test was used for the comparison of the means in the normally distributed data, and the Mann–Whitney *U* test was employed for the comparison of the mean of the ranks where the data distribution was not normal. The χ^2 analysis was utilized for the comparison of the frequencies between the 2 groups. Repeated-measures analysis of variance was used when the comparison of specific outcomes over a time course was intended in the case of the normal distribution of the data, while the Friedman test was used in the case of the deviation of the data distribution from normal. The power of analysis was 80%, and the level of significance was 0.05.

RESULTS

Fifty-two patients at a mean age of 17.14±12.5 months were recruited for this study. The complete demographic information and the clinical variables such as the duration of surgery, the cross-clamp time, the duration of mechanical ventilation, and the length of ICU stay are summarized in Table 1. The frequency of the congenital anomalies is described in Table 2. The most prevalent anomaly was the tetralogy of the Fallot with a prevalence rate of 25%.

Table 1. Demographic variables and the clinical outcomes of the study

	Mean± SD	Range
Age (mon)	17.14±12.5	2-50
Weight (kg)	9.01±2.98	4-15.50
Height (cm)	81.33±19.33	56-115
Operation duration (min)	297.02± 59.15	210-500
CPB time (min)	191.25±34.5	55-195
Cross-clamp time (min)	75.48±31.88	26-140
Mechanical ventilation (min)	21.78±18.31	3-96
ICU stay (h)	133.3±97.68	46-600

CPB, Cardiopulmonary bypass; ICU, Intensive care unit

Table 2. Frequency of the anomalies indicated for surgical resection in the study population

Diagnosis	Frequency	Frequency %
TF	13	25
VSD and PS	4	7.7
VSD	8	15.4
CAVSD	3	5.8
Truncus arteriosus	2	3.8
PS	1	1.9
TAPVC	3	5.8
APW	2	3.8
ASD and VSD	3	5.8
AVSD	1	1.9
PAPVC	1	1.9
AS	4	7.7
TCPC	1	1.9
VSD+PH	2	3.8
ALCAPA	1	1.9
TF + PDA	1	1.9
VSD and valvular repair	1	1.9
CAVCD	1	1.9

TF, Tetralogy of Fallot; VSD, Ventricular septal defect; CAVSD, Complete atrioventricular septal defect; PS, Pulmonary stenosis; TAPVC, Total anomalous pulmonary venous connection; APW, Aortopulmonary window; ASD, Arterial septal defect; AVSD, Atrioventricular septal defect; PAPVC, Partial anomalous pulmonary venous connection; AS, Aortic stenosis; TCPC, Total cavopulmonary connection; PH, Pulmonary hypertension; ALCAPA, Anomalous left coronary artery from the pulmonary artery; PDA, Patent ductus arteriosus; CAVCD, Complete atrioventricular canal defect

Consecutive measurements of the pro-BNP level demonstrated a decreasing trend by comparison from the first measurement at the time of admission until 48 hours after transfer

to the ICU. Thereafter, the level started to decrease until to 72 hours after transfer to the ICU (Fig. 1). Next, the correlations between the pro-BNP level and the duration of mechanical ventilation and the length of stay at the ICU were tested (Table 3). The results revealed that that the pro-BNP level from ICU admission until 48 hours after ICU entrance was directly correlated with the ICU length of stay.

After the patients were divided into 2 subgroups of the extubation time at least 12 hours after surgery and the extubation time less than 12 hours after surgery, the groups were compared in terms of the demographic information and the other clinical variables (Table 4). The level of plasma lactate at ICU entrance was significantly higher in the group with the extubation time less than 12 hours after surgery (2.27±0.68 vs 1.79±0.68; *P*=0.027). The pro-BNP values did not demonstrate significant differences between the 2 groups.

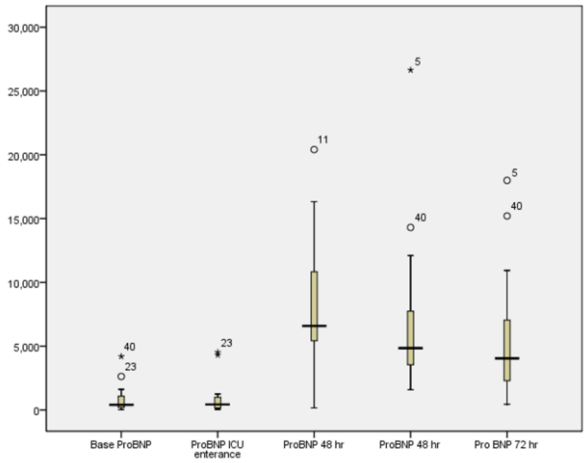

Figure 1. Trend of the changes in the level of pro-BNP from the time of anesthesia induction until 72 hours after transfer to the intensive care unit

Table 3. Correlation between the circulatory pro-BNP level at different times and the duration of mechanical ventilation and the length of stay at the ICU

Pro-BNP Measurements (ng/mL)						
		Baseline	**ICU Entrance**	**24 h post ICU**	**48 h post ICU**	**72 h post ICU**
Mechanical ventilation	Correlation coefficient	0.158	0.258	0.259	-0.009	0.030
	P	0.317	0.093	0.086	0.255	0.890
ICU stay	Correlation coefficient	0.244	0.313*	0.309*	0.338*	0.308
	P	0.126	0.031	0.044	0.046	0.129

*P<0.05 for the Pearson correlation test
BNP, Brain natriuretic peptide; ICU, Intensive care unit

Table 4. Comparison of the demographic information and the main outcome variables between the 2 study groups regarding the extubation time

	Extubation Time ≥12 h (n=28)	**Extubation Time < 12 h (n=17)**	*P*
Age (mon)	17.51±14.25	18.25±10.73	0.860
Height (cm)	78.66±16.58	70.25±10.90	0.401
Weight (kg)	8.24±2.96	10.37±2.26	0.024*
Gender (male)	17 (61%)	12 (71%)	0.541
CPB duration (min)	127.1±38.8	114.5±27.3	0.267
Operation time (min)	293.5±46.3	303.8±84.0	0.602
Cross-clamp time (min)	74.1±36.5	67.9±27.2	0.701
ICU stay (h)	131.2±66.4	96.1±65.0	0.107

* P<0.05 in between-group comparisons
CPB, Cardiopulmonary bypass

Table 5. Comparison of the clinical laboratory parameters between the 2 study groups regarding the extubation time

	Extubation Time ≥12 h (n=28)	Extubation Time < 12 h (n=17)	*P*
Preoperative pro-BNP	375(181-1228)	250(37-558)	0.058*
Pro-BNP ICU (pg/mL)	428(168-1186)	307(164-694)	0.206*
Pro-BNP 24 h (pg/mL)	7625±6124	5571±3193	0.152
Pro-BNP 48 h (pg/mL)	4398(1984-4646)	7746(5144-19376)	0.959*
Preoperative lactate (mg/dL)	0.69±0.63	0.91±0.31	0.795
ICU lactate (mg/dL)	1.79±0.68	2.27±0.68	0.027
ICU lactate 24 h (mg/dL)	1.05(0.90-2.17)	1.1(1.07-1.22)	0.749*
ICU lactate 48 h (mg/dL)	0.95(0.72-1.17)	0.80(0.61-1.07)	0.289*
Preoperative pH	7.35(7.32-7.43)	7.34(7.28-7.38)	0.751*
ICU pH	7.38±0.08	7.40±0.06	0.378
pH 24 h	7.37±0.09	7.41±0.05	0.424
pH 48 h	7.42±0.04	7.44±0.05	0.143
Preoperative BE	-3.85±3.71	-5.34±2.82	0.178
ICU BE	4.07±3.27	-3.91±4.29	0.790
BE 24 h	1.91±3.90	0.88±3.62	0.721
BE 48 h	2.96±4.17	1.29±3.56	0.228

* These variables followed non-normal data distributions, and the *P* values were calculated with the Mann–Whitney *U* test for these variables in the between-group comparisons. Descriptive data for the variables with normal distributions are described as means ± standard deviations (SDs) and for the variables with non-normal distributions as medians (Q1–Q3).
BNP, Brain natriuretic peptide; ICU, Intensive care unit

DISCUSSION

In the present study, we assessed the relationships between the circulatory pro-BNP level and the duration of postoperative mechanical ventilation, the length of stay at the ICU, the duration of surgery, the duration of CPB, and the aortic cross-clamp time. There was no correlation between the duration of mechanical ventilation and the circulatory pro-BNP level measured at preoperative times; at ICU entrance; and 24, 48, and 72 hours after surgery. We also found a direct correlation between the circulatory pro-BNP levels at the time of ICU entrance and 24 and 48 hours after surgery and the length of stay in the ICU. There were no significant differences between our 2 study subgroups of the extubation time less than 12 hours after surgery and the extubation time at least12 hours after surgery in terms of pro-BNP at all the study time points. However, the patients in the former subgroup had a higher blood lactate level at ICU admission.

In a study by Koch et al,[24] no significant correlation was found between the postoperative plasma BNP level and parameters such as the ICU length of stay, the mechanical ventilation duration, and the use of inotropic and diuretic drugs. The authors concluded that in children who experience a rise in the BNP level immediately after surgery, this increase is correlated with a higher duration of CPB and a higher circulatory lactate level. In contrast, in the current study, we observed a significant direct correlation between the circulatory pro-BNP level at preoperative times and 24 and 48 hours after surgery on the one hand and the length of stay at the ICU on the other. A study by Berry and colleagues[25] investigated the BNP prognostic value in patients undergoing palliative surgeries for congenital single-ventricle defects. According to the findings of that study, the plasma pro-BNP level at 6 to 12 hours postoperatively had a role in predicting the length of hospital stay (P=0.005) and the need for inotropic drugs (P=0.001). In contrast, we observed that the pro-BNP levels at the time of admission to the ICU and 24 and 48 hours after the operation were significantly correlated with the length of stay at the ICU. Nonetheless, the length of hospital stay was not investigated in this study.

A study by Hsu et al[26] investigated the predictive value of type B natriuretic peptide for postsurgical outcomes in neonatal cardiac surgery. In that study, the patients were divided into 2 groups. While the patients in the first group underwent palliative surgery, those in the second group were treated with restoration surgery. Both groups of patients were sampled at preoperative times, 2 hours after surgery, and then 12 and 24 hours after surgery to measure BNP. The authors measured outcomes such as mortality, the need for reoperation before discharge, the need for cardiac transplantation up to 6 months after surgery, mechanical ventilation, and the postoperative low cardiac output syndrome and reported an association between a rise in the level of BNP at 24 hours postoperatively compared with the preoperative time (baseline) and an increased duration of mechanical ventilation. Young et al[27] conducted a systematic review to identify the predictive value of plasma BNP for postoperative cardiac complications and concluded that the current evidence supported the usefulness of the level of BNP for the risk stratification of patients during surgery and taking proper measures to manage major adverse cardiac events during and after surgery.[28]

CONCLUSIONS

In the present study, higher serum pro-BNP levels at the time of ICU admission and 24 and 48 hours after admission were related to a prolonged ICU stay. However, the serum BNP level was not correlated with the duration of mechanical ventilation after pediatric cardiac surgery.

Limitations

The heterogeneity of cardiac procedures and surgeons may affect the operation outcome and also the duration of mechanical ventilation and the length of stay at the ICU. We were not able to adjust this confounding factor. This investigation was a single-center study, and the institutional protocols in CPB management and weaning from the ventilator might have affected the results.

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