

## Does B-type Natriuretic Peptide Level Predict Outcome After Arterial Switch Operation ?

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**Evaluation the predictive value of perioperative Plasma B-type natriuretic peptide level in arterial switch operation.** Plasma B-type natriuretic peptide level was measured before and 24 hours after surgery in 29 patients with arterial switch operation. We evaluated 29 patients (22 male,76%,7 female 24%) with mean age  $67.93 \pm 84.09$  days (range 6 days to 14months).The mean of BNP level before surgery was  $7989.96 \pm 9691.94$  and increased after surgery to  $22391.35 \pm 11898.67$  and difference between two groups was significant ( $P=0.003$ ).In linear regression test the BNP did not correlate with sex( $r=0.33$ ,  $P=0.085$ ) and age( $r=0.14$ , $P=0.45$ ). Furthermore, BNP did not correlate with duration of mechanical ventilation ( $r=0.132$ , $P=0.53$ ) , ICU stay ( $r=0.137$ , $P=0.52$ ) and with lactate level ( $r=0.41$ , $P=0.054$ )after operation. During the study 4 patients(13.8%) died and the mean of BNP 24h after operation among them was  $35000.00 \pm 00.00$ .using chi-square and fisher exact test the correlation between BNP and death was significant( $P=0.001$ ). We implied that BNP level increased 24 hours after arterial switch operation, moreover we denoted it correlated well with the death rate and an increase in B-type natriuretic peptide 24 hours after surgery predicts poor postoperative outcome. However it did not correlate with duration of mechanical ventilation ,ICU stay and lactate level in this patients.

**Keywords:** BNP, arterial switch operation, duration of mechanical ventilation.

B-type natriuretic peptide (BNP) is a cardiac neurohormone secreted from membrane granules in the cardiac ventricles as a response to ventricular volume expansion and pressure overload. BNP is a 32-amino acid polypeptide hormone, with diuretic, natriuretic, and vasoactive actions, and use as a biomarker for the management of cardiac disease in both pediatric and adults' patients<sup>1-4</sup>.

Recently a study in patients with

congenital heart defects amenable to biventricular repair indicated that measurement of circulating levels of BNP can predict the development of low cardiac output syndrome (LCOS) and prolonged mechanical ventilation (5).Furthermore, other studies indicated higher plasma level of BNP in children with congenital heart disease and newborns with severe fetal distress (6-8).Because of serious complications related to congenital cardiac defects, surgical repair or palliation of congenital cardiac defects is carried out usually during the neonatal period (8-9).Moreover, neonates, compared to infants and children, have more adverse events and perioperative mortality.

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On the other hand, the clinical predictive value of perioperative plasma BNP levels in neonates, who are most at risk for unpredictable adverse outcomes, is controversial<sup>5-10</sup>. So, we steered this study to address these concerns and to shed light on predictive value of preoperative BNP plasma level in patients under cardiac surgery.

## MATERIALS AND METHODS

We directed a prospective cohort study in the Rajaiee cardiac hospital at the Tehran University of medical sciences between May 2012 and September 2012. The study protocol was approved by ethical committee of Tehran University of medical sciences. Furthermore, we obtained written informed consent from the patients' parents or guardians before enrollment in the study.

Eligible patients were children with TGA undergoing arterial switch operation. The preoperative anesthesia management, intraoperative bypass strategy, and subsequent Pediatric Cardiac Intensive Care Unit management followed standard institutional practices. All patients underwent modified ultrafiltration before separating from CPB. An on-service team, blinded to the BNP values, made all patient management decisions.

### Data Collection

Blood samples were obtained from an arterial catheter 2 hours before operation and 24 hours after CPB. The samples were placed immediately on ice in chilled ethylenediaminetetraacetic acid tubes and centrifuged at 3000 rpm for 15 minutes at 4°C.

Separated plasma was stored at -20°C. Within 4 days of obtaining the sample, the plasma was thawed to room temperature and BNP levels were measured using a commercially available fluorescence immunoassay (Triage Meter Plus,

Biosite Diagnostic, San Diego, Calif). The measurable range of BNP on this device is between 5 and 5000 pg/mL. The estimated coefficient of variation for the assay is 9.2% to 11.4%.

Clinical and biochemical data were collected prospectively at each sampling point and daily thereafter by an observer blinded to the BNP data. The clinical data collected included the patient demographics, CPB duration, aortic cross clamp duration, inotrope dose, intensive care unit days, hospital days, and use of

mechanical ventilation. Biochemical data collected included Hb, BS, serum lactate, blood urea nitrogen, and creatinine level.

### Statistical analyses

Data were analyzed using SPSS version 20. Categorical data are presented as numbers (%), and continuous data as mean  $\pm$  SD. We used the Chi<sup>2</sup> or Fisher's exact test to compare categorical variables and the Student's *t* test, the paired *t* test, or the Mann-Whitney's rank sum *U* test to compare continuous variables. Correlations between BNP concentrations and hemodynamic variables were calculated by Spearman rank correlation analysis.

## RESULTS

In this study we evaluated 29 children (22 boy, 76%, 7 girls 24%) with mean age 67.93 $\pm$ 84.09 days (range 6 days to 14 months). The patients' main cardiac lesions were VSD, ASD, dTGA, PDA. All patients after operation needed inotropic agents as epinephrine, milrinone, dobutamine, adrenaline and dopamine.

The mean of BNP before surgery was 7989.96 $\pm$ 9691.94 and increased after surgery to 22391.35 $\pm$ 11898.67 and difference between two groups was significant ( $P=0.003$ ) (Table 1). In linear regression test the BNP did not correlate with sex ( $r=0.33, P=0.085$ ) and age ( $r=0.14, P=0.45$ ). Furthermore, BNP did not correlate with ventilation

**Table 1 .** BNP, BUN and Cr pre and post operation

	pre	post	Pvalue
BNP	7989.96 $\pm$ 9691.94	22391.35 $\pm$ 11898.67	0.003
BUN	9.47 $\pm$ 3.43	10.35 $\pm$ 3.77	0.30
Cr	0.57 $\pm$ 16	0.60 $\pm$ 0.32	0.35

time ( $r=0.132, P=0.53$ ), ICU stay ( $r=0.137, P=0.52$ ) and with lactate level ( $r=0.41, P=0.054$ ) after operation. During the study 4 patients (13.8%) died and the mean of BNP 24 after operation among them was  $35000.00 \pm 00.00$ . using chi-square and fisher exact test the correlation between BNP and death was significant ( $P=0.001$ ).

**Table 2.** The mean and SD of variables

variables	Mean	SD
Hb	14.14	2.84
BS	76.10	15.36
Pomp duration	164.00	44.90
Clamp	102.41	32.95
Transfusion during operation	182.69	116.80
Lactate*	5.29	2.75
Lactate*	3.90	2.54
Lactate*	3.30	2.04
Lactate*	2.93	1.72
Lactate**	2.77	1.58
Lactate**	1.88	1.78
Ventilation post operation(hour)	82.46	72.59
ICU stay(day)	7.41	3.56
Bleeding post operation	53.27	91.42
Transfusion post operation	70.17	74.05

\*lactate one day after operation every 6 hours

\*\*lactate two days after operation every 12 hour

## DISCUSSION

There are little evidences to suggest that BNP may be helpful in a pediatric clinical setting<sup>11</sup>. However, it is clear that it increases in various pathologic states; particularly those involved in increased cardiac chamber wall stretch and expanded fluid volume as heart failure, renal failure, primary hyperaldosteronism, and in reduced peptide clearance as in renal failure<sup>11, 12</sup>. Furthermore some studies indicated that BNP seems to have clinical utility in terms of excluding the diagnosis of heart failure in patients with symptoms of breathlessness or fluid retention and may provide prognostic information about those with heart failure or other cardiac diseases<sup>13-18</sup>. Also, there is some evidence that it may be useful for monitoring heart failure therapies<sup>19-20</sup>.

Ootaki *et al* in a study indicated that plasma BNP levels correlate well with biventricular volume, particularly with left ventricular volume in

various congenital heart diseases such as atrial septal defect, ventricular septal defect, and tetralogy of fallot and with cyanotic heart diseases<sup>21</sup>.

Furthermore in another survey, Suda *et al.* signified that plasma BNP level reflects pressure and volume loading of the right ventricle and the pulmonary artery, so, they purposed that BNP determinations may help to identify children with ventricular septal defect complicated by pulmonary hypertension, which needs urgent intervention<sup>22</sup>. These findings recommend that BNP may be a valuable biomarker for prognostication and risk stratification in neonates undergoing cardiac surgery and the measurement of plasma BNP may add clinically useful information relevant to the management of children with congenital heart disease.

In this clinical trial we indicated that the mean of BNP 24 hours after operation significantly increased ( $7989.96 \pm 9691.94$  vs.  $22391.35 \pm 11898.67$ ,  $P=0.003$ ), moreover in four patients that died after operation the mean of BNP plasma level was higher than other (35000 vs. 22391) and the correlation between death and BNP was significant ( $p=0.001$ ). In agreement to our results Koch *et al.* in a study signified that in children with congenital heart defects plasma BNP level increased immediately after cardiac surgery<sup>23</sup>. Moreover another study by **Shih *et al.*** showed B-type natriuretic peptide levels increased after separation from cardiopulmonary bypass, with an 8-fold peak increase at 12 hours<sup>24</sup>. However, in contrast to our results HSU *et al* evaluated the plasma B-type natriuretic peptide levels in 36 consecutive neonates and indicated that B-type natriuretic peptide levels at 24 hours were lower than preoperative levels<sup>12</sup>. Moreover Sanjeev *et al.* in another survey specified that elevation of plasma BNP accurately detects the presence of PDA in premature infants. Also, they designated that successful closure is reflected by a corresponding decrease in BNP plasma level in neonates<sup>25</sup>. A possible explanation for such a discrepancy between studies is heterogeneity in patient's samples and different technique in BNP measurement.

Our results did not show any correlation between BNP and serum lactate and duration of mechanical ventilation after surgery and BNP but conversely, Sanjeev *et al.* in their review pointed out

that cardiopulmonary bypass time and serum lactate concentration correlated to BNP<sup>25</sup>. Moreover, Shih et al showed postoperative 12-hour B-type natriuretic peptide levels were related with the duration of mechanical ventilation and low cardiac output after surgical treatment<sup>24</sup>.

During the study 4 patients died and the mean of BNP 24hours after operation among them was more than 35000 that is higher than other patients, more over death rate significantly correlate with BNP plasma level. In line with our outcomes Price et al. in a study pointed out that BNP concentrations increase in children with chronic LV systolic dysfunction and predict the 90-day composite end point of death, hospitalization, or listing for cardiac transplantation<sup>26</sup>.

The main limitations are inherent to the present study are the relatively small sample size and short duration of follow-up. Further investigations are recommended with longer follow-up and larger series to validate the findings reported here.

### CONCLUSION

we implied that BNP plasma level increased 24 hours after surgical intervention in children with congenital heart disease, moreover we denoted it correlated well with the death rate and an increase in B-type natriuretic peptide 24 hours after surgery predicts poor postoperative outcome. However it did not correlate with ventilation time and lactate level in this patients.

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