Alterations in plasma B-type natriuretic peptide levels after repair of congenital heart defects: A potential perioperative marker

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Objectives: B-type natriuretic peptide, a cardiac hormone with diuretic, natriuretic, and vasoactive properties, is used in the diagnosis, risk stratification, and management of adult cardiac patients. However, no study has yet determined the prognostic value of B-type natriuretic peptide after surgical intervention for congenital heart disease. The objectives of this study were (1) to determine alterations in B-type natriuretic peptide levels after repair of congenital heart disease with cardiopulmonary bypass and (2) to investigate potential associations between B-type natriuretic peptide levels and outcomes in this patient population.

Methods: Fifty-one infants and children undergoing repair of congenital heart disease were studied. B-type natriuretic peptide levels were measured before and after surgical intervention, and the ability of the postoperative 12-hour B-type natriuretic peptide level to predict postoperative outcomes was evaluated.

Results: B-type natriuretic peptide levels increased after separation from cardiopulmonary bypass, with an 8-fold peak increase at 12 hours ($P < .005$). Postoperative 12-hour B-type natriuretic peptide levels were associated with the duration of mechanical ventilation and the presence of a low cardiac output state after surgical intervention. On multivariate analysis, the 12-hour B-type natriuretic peptide level was an independent predictor of the duration of mechanical ventilation. In fact, B-type natriuretic peptide levels of greater than 540 pg/mL predicted mechanical ventilation beyond 48 hours, with a sensitivity of 88.9% and a specificity of 82.5%. In addition, B-type natriuretic peptide levels of greater than 815 pg/mL predicted the presence of a low cardiac output state within 48 hours after surgical intervention, with a sensitivity of 87.5% and a specificity of 90.2%.

Conclusions: B-type natriuretic peptide determinations might be a useful tool for clinicians caring for infants and children after surgical intervention for congenital heart disease.

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Despite numerous advances, surgical intervention for patients with congenital heart disease continues to carry significant morbidity and mortality. Accordingly, considerable resources, including specialized intensive care, are used postoperatively, and yet up to 25% of infants and young children have diminished cardiac output within the first 24 hours.[1,2] Management during this period is complicated by a dearth of validated physiologic markers to guide therapy, resulting in a substantial reliance on subjective clinical assessments. Direct measurements of hemodynamic indices, such as cardiac output, are often not possible in these patients because of altered blood flow (eg, intracardiac shunting), size limitations that preclude invasive monitoring, or both, making the continued search for such reliable markers important.

Abbreviations and Acronyms
BNP = B-type natriuretic peptide
CHF = congestive heart failure
CPB = cardiopulmonary bypass
PCICU = Pediatric Cardiac Intensive Care Unit
Svo_2 = mixed venous oxyhemoglobin saturation

B-type natriuretic peptide (BNP) is a 32-amino-acid polypeptide hormone with diuretic, natriuretic, and vasoactive properties that is secreted by the cardiac ventricles in response to myocyte stretch.[3] Determinations of BNP are increasingly used in the diagnosis, risk stratification, and management of adult cardiac patients.[4-7] Much less data exist on the role of BNP in pediatric patients with cardiac disease, and no study has yet determined the prognostic value of BNP levels after surgical repair of structural congenital heart defects.[8-13]

The objectives of this study were thus (1) to determine alterations in BNP levels over time after repair of congenital heart defects with cardiopulmonary bypass (CPB) and (2) to investigate potential associations between BNP levels and outcomes in this patient population. We prospectively studied 51 infants and children undergoing complete repair of structural congenital heart defects with CPB. Systemic arterial plasma BNP determinations were made before and 2, 12, and 24 hours after CPB. We then evaluated the ability of the 12-hour BNP level to predict postoperative outcomes.

Methods

Subjects

This prospective cohort study was conducted at the Pediatric Cardiac Intensive Care Unit (PCICU) at the University of California, San Francisco. Patients with congenital heart defects undergoing complete surgical repair with CPB were enrolled. Patients were excluded from the study if they required staged single-ventricle palliation or were unable to separate from CPB and required extracorporeal life support postoperatively.

The patients were followed up during their entire course in the PCICU. The perioperative anesthesia management, CPB strategy, and subsequent PCICU management followed standard institutional practices. After surgical repair, all patients were admitted to the PCICU intubated and mechanically ventilated. An on-service team that was blinded to the BNP values made all decisions regarding patient management.

Written informed consent was obtained from the patients' parents or guardians before enrollment of the patients into the study. The institutional review board at the University of California, San Francisco, reviewed and approved this study.

Data Collection

Blood samples were obtained from an arterial catheter preoperatively and at 2, 12, and 24 hours after CPB. The samples were immediately placed on ice in prechilled ethylenediamine tetraacetic 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 with a commercially available fluorescence immunoassay (Triage Meter Plus, Biosite Diagnostic). The measurable range of BNP on this device is between 5 and 5000 pg/mL. The average 95% confidence limit of the analytic sensitivity for the Triage BNP test is less than 5 pg/mL.

Clinical and laboratory data were prospectively collected at each sampling point and once daily thereafter by an observer blinded to the BNP data. The clinical data collected included demographics, CPB time, crossclamp time, duration of mechanical ventilation, inotrope dosage, mean systemic arterial pressure, central venous pressure, and fluid balance. Laboratory data included base deficit, venous blood gases, and serum lactate levels.

Preoperative Classification of Cardiac Defect

Cardiac lesions were classified as having decreased, normal, or increased pulmonary blood flow to investigate associations between preoperative BNP levels and preoperative cardiac physiology. Lesions classified as having decreased pulmonary blood flow included pulmonary atresia, tetralogy of Fallot, and pulmonary stenosis. Lesions classified as having increased pulmonary blood flow included atrial septal defect, ventricular septal defect, atrioventricular septal defect, truncus arteriosus, transposition of the great arteries, and totally anomalous pulmonary venous return.

Calculations

Inotrope use was quantified by a score adapted from Wernovsky and colleagues.[2] The score was calculated by obtaining the total amount of inotropic support the patients received at each sampling point and then entering the data into the following equation:

$$Dopamine + Dobutamine + ([Epinephrine + Norepinephrine] \times 100) = Milrinone \times 20).$$

Units of inotrope dosage used in this equation were in micrograms per kilogram per minute.

The definition of a low cardiac output state was identical to criteria published by Hoffman and coworkers.[1] Low cardiac output state was defined by a combination of changes in clinical signs and biochemical indicators and the administration of interventions aimed at augmenting cardiac output, including increased pharmacologic support relative to the baseline and mechanical pacing. Clinical signs included tachycardia, oliguria, poor perfusion, or cardiac arrest occurring with or without a widened arterial–mixed venous oxyhemoglobin saturation (Svo_2) difference or metabolic acidosis.

Analysis of the Data

Analysis of continuous variables within categories was made with *t* tests and analysis of variance or the nonparametric Mann-Whitney and Kruskal-Wallis tests, as appropriate. Because of their nonnormal distribution, BNP levels were log transformed. A linear regression model was used to assess the association between the log-transformed 12-hour BNP levels and the primary predictor (ie, the duration of mechanical ventilation). A logistic regression model was used to assess the association between 12-hour BNP