Role of Brain Natriuretic Peptide in Detection of Right Ventricular Dysfunction and Pulmonary Hypertension among Children with Chronic Lung Diseases

Thesis

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Nora Waheed Hassan Mohamed

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Abb.	Full term
6MWT	*6-min walk test*
A'	*Annular peak velocity during late diastole.*
ACC/AHA	*American College of Cardiology/American Heart Association.*
ACE	*Angiotensin converting enzyme*
AD	*Autosomal dominant.*
AO	*Aortic bulb.*
Aort VTI	*Time velocity integral foe aortic valve.*
AORT-VTI	*Time velocity integral for aortic valve.*
AR	*Autosomal recessive.*
ARDS	*Adult respiratory distress syndrome*
AT/PEAET	*Acceleration time/ pulmonary artery ejection time.*
BAL	*Bronchoalveolar lavage*
BNP	*Brain natriuretic peptide*
CAD	*Coronary artery disease*
CBC	*Complete blood count.*
CF	*Cystic fibrosis.*
chILD	*Children's interstitial lung disease*
CI	*Cardiac index.*
CNP	*Natriuretic peptide receptor-C.*
COPD	*Chronic obstructive pulmonary disease*
CRP	*C-reactive protein.*
CRT	*Cardiac resynchronization therapy*
CRT	*Cardiac resynchronization therapy.*
CTD	*Connective tissue disease*
CTD	*Connective tissue disease.*
CXRs	*Chest x-rays.*
DT	*Deceleration time.*
E'	*Annular peak velocity during early diastole.*

List of Abbreviations (Cont...)

Abb.	Full term
E/A	*Ratio between heights of early and late diastolic flow velocity peaks for both mitral and tricuspid valves.*
ECHO	*Echocardiography.*
ECM	*Extra cellular matrix.*
EDV	*End diastolic volume.*
EF%	*Ejection fraction.*
ELISA	*Enzyme-linked immunosorbent assay*
eNO	*Exhaled nitric oxide*
ESR	*Erythrocyte sedmintation rate.*
ESV	*End systolic volume.*
ESWSm	*end-systolic wall stress*
ESWSm	*Left ventricular meridional end-systolic wall stress.*
ET	*Ejection time*
ET-MV	*Ejection time mitral valve.*
ET-TV	*Ejection time tricuspid valve.*
FDA	*Food and Drug administration*
FEV1	*Forced expiratory volume in one second.*
FS%	*Fractional shortening.*
FVC	*Forced vital capacity*
HB	*Haemoglobin.*
HIV	*Human Immunodeficiency virus*
HP	*Hypersensitivity pneumonitis*
HP	*Hypersensitivity pneumonitis.*
HRCT	*High-resolution computed tomography*
Ht	*Height*
Ht	*Height.*
IgA	*Immunoglobulin A*
IgG	*Immunoglobulin G*
IIP	*Idiopathic interstitial pneumonia*

List of Abbreviations (Cont...)

Abb.	Full term
ILD	*Interstitial lung disease*
ILDs	*Chronic interstitial lung diseases.*
Indexed RA area	*Indexed right atrium area.*
IPF	*Interstitial pulmonary fibrosis.*
IV	*Administered intravenously.*
I.V	*Intravenously*
IVCT	*Isovolumetric contraction time*
IVMA-MA	*Mitral valve myocardial acceleration during isovolumetric contraction.*
IVMA-MV	*Mitral valve myocardial acceleration during isovolumic contraction.*
IVMA-PA	*Pulmonary artery*
IVMA-TV	*Tricuspid valve myocardial acceleration during isovolumetric contraction.*
IVRT	*Isovolumetric relaxation time*
IVSD	*Interventricular septum thickness at end-diastole.*
IVSS	*Interventricular septum thickness at end-systole.*
KL-6	*Krebs von den Lunge-6 antigen*
LA	*Left atrium.*
LTx	*Lung transplantation*
LV	*Left ventricle.*
LVED	*Left ventricular end diastolic dimension.*
LVEDPs	*LV end-diastolic pressures*
LVES	*Left ventricular end systolic dimension.*
LVIDd	*Left ventricular internal dimension at end-diastole.*
LVIDs	*Left ventricular internal dimension at end-systole.*
LVM	*Left ventricular mass.*

List of Abbreviations (Cont...)

Abb.	Full term
LVP Wd	*Left ventricular posterior wall thickness at end-diastole.*
LVP Ws	*Left ventricular posterior wall thickness at end-systole.*
LVRWT	*Left ventricular relative wall thickness.*
LVWI	*Left ventricular work index.*
MMP	*Matrix metalloproteinases*
mMRC	*Modified Medical Research Council*
MPI	*Myocardial performance index*
MPV	*Mean platelet volume.*
MRI	*Magnetic resonance imaging*
OLB	*Open lung biopsy*
OLB	*Open lung biopsy.*
PA VTI	*Time velocity integral for pulmonary valve.*
PAH	*Pulmonary arterial hypertension.*
PaO_2	*Partial pressure of oxygen*
PAP	*Pulmonary artery pressure.*
PA-VTI	*Time velocity integral for pulmonary artery.*
PDE5	*Phosphodiesterase type 5*
PDE5	*Phosphodiesterase type 5 inhibitors.*
PPH	*Persistent pulmonary hypertension.*
PVR	*Peripheral vascular resistance.*
RHC	*Right heart catheterization.*
ROC	*Receiver operating characteristic curve.*
RPEP/AT	*Right ventricle pre -ejection period/right ventricle acceleration time.*
R-sist	*Right ventricular systolic time.*
RSV	*Right ventricular stroke volume.*
RV MPI	*Right ventricle myocardial performance index.*
RV S/D ratio	*Right ventricle systolic/diastolic ratio.*
RV WI	*Right ventricular work index.*

List of Abbreviations (Cont...)

Abb.	Full term
RV-FAC	*Right ventricle fractional area change.*
RVPEP/RVET	*Right ventricule pre-ejection period/ right ventricle ejection time.*
RVRWT	*Right ventricular relative wall thickness.*
RVWL	*Right ventricular work index.*
S'	*Annular peak velocity during systole.*
SC	*Subcutaneously*
SD	*Standard deviation.*
SFmid	*Midwall Shortening Fraction*
SPSS	*Statistical program for social science.*
SV	*Stroke volume.*
TAPSE	*Tricuspid annular plane systolic excursion.*
TDI	*Tissue doppler imaging.*
Tej	*Pulmonary ejection time.*
TLC	*Total leucocytic count.*
TTE	*Transthoracic echocardiography*
UPPP	*Uvulopalatopharyngoplasty*
VATS	*Video assisted thoracoscopy.*
Wt	*Weight.*

Abstract

Background: Pulmonary arterial hypertension (PAH) is an important determinant of morbidity, mortality and severity in chronic lung diseases children. Echocardiography is an indirect measure for PH with a limited accuracy compared to right heart catheterization and requires qualified physicians. BNP is the major hormone of the natriuretic peptide system, which is highly activated in different left and right heart diseases in the context of neurohumoral activation. In addition, in pulmonary arterial hypertension, BNP levels are elevated and seem to reflect clinical and hemodynamic status in this patient population. So, the aim of current study to detect the role of BNP in detection of pulmonary hypertension in CLDs children as objective, easy, repeatable available method.

Methods: Case-control study on thirty (30) children with Chronic lung diseases who recruited from the Pediatric chest clinic, Children hospital, Ain Shams University. We classified patients into PH and non-PH groups according to echocardiographic measurement of PAP >25mmHg.Serum BNP was assessed and correlated to echocardiographic data.

Results: Serum BNP showed a highly statistically significant difference between two groups. AS, mean level of BNP in PH group compared to non-PH group was (265.30±199.83 &40.01±23.01) respectively. Moreover, BNP significantly correlated with Echocardio-graphic parameters that reflect RT ventricular dysfunction. BNP cut-off to diagnose PH among studied patients was > 97.5 pg/ml with sensitivity of 95%, specificity of 98%, PPV equals 98%, NPV equals 94% and accuracy 98%.

Conclusion: BNP is an objective, repeatable, easy marker can be used to diagnose pulmonary hypertension in chronic lung diseases in children.

Keywords: B-type natriuretic peptide; pulmonary hypertension; chronic lung diseases; Paediatrics; ECHO.

INTRODUCTION

Pediatric chronic lung diseases include many diseases such as: bronchiectasis, interstitial pulmonary fibrosis, cystic fibrosis, asthma, emphysema, bronchopulmonary dysplasia, sequestrated lung disease and bronchiolitis obliterans. They can be primary or secondary. They can be congenital or acquired ***(Ibrahim et al., 2011).***

They represent a heterogeneous group of many distinct clinicopathological entities. Their prevalence have increased in the past decade because of the more advanced and intensive respiratory support provided for compromised children ***(Rossi and Owens, 2005).***

Children with chronic diseases of the respiratory system represent a large and even growing population, there is a need for an early and reliable diagnosis of complicating pulmonary hypertension (PH) leading to additional dyspnea and increased mortality ***(Hanno et al., 2006).***

Incessant exposure to hypoxemia is one of the mechanisms besides others leading to sustained pulmonary vasoconstriction and narrowing of the pulmonary vasculature. Consequently, PH develops leading to right heart enlargement with ventricular hypertrophy, and impaired cardiac function, known as corpulmonale**.** Although PH potentially develops in every hypoxemic or chronic lung disease, there is still

uncertainty about the degree of a clinical relevant PH and about the time point when right heart catheterization should be initiated, as this is the method of choice to definitely diagnose PH ***(Weitzenblum, 2003).***

The most accurate method for early diagnosis of PH is right heart catheterization, but it still dangerous and invasive technique, Echocardiography (ECHO) is an important modality in the noninvasive assessment of PH and has been used to screen for the disease, determine right and left heart structure and function, and assess response to therapy in persons with PH ***(Galie et al., 2004).***

Although limitations to its use in PH and PAH exist, several aspects of ECHO are particularly helpful in the assessment and long-term management of patients with PH ***(McGoon et al., 2004).***

BNP is the major hormone of the natriuretic peptide system, which is highly activated in different left and right heart diseases in the context of neurohumoral activation. BNP is of special interest in this field as it is predominately secreted by the cardiac ventricles. In addition, in pulmonary arterial hypertension, BNP levels are elevated and seem to reflect clinical and hemodynamic status in this patient population. There are other studies that compare between BNP and catheterization in diagnosis of PH but did not compare data