Elevated B-Type Natriuretic Peptide Blood Levels during Hypertensive Crisis A Novel Diagnostic Marker of Acute Coronary and Cerebrovascular Events

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By

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ABSTRACT

Background:- It is not so easy to make a quick screening between hypertensive emergency (H.E) and hypertensive urgency (H.U), as it often requires sophisticated, complex and time consuming clinical, instrumental and diagnostic tests.

Aim:- To address the role of B-type natriuretic peptide (BNP) in hypertension and how to use it to differentiate H.E from H.U to alleviate possible complications.

Methods:- A total of 30 patients with rapid severe elevation of blood pressure (B.P) admitted to the inpatient wards and critical care department, Cairo University, were included in a prospective, non-interventional study. On the basis of the clinical findings, patients were subdivided into two groups: **Group I:-** 15 patients with H.E with acute organ involvement and **group II:** 15 patients with H.U without acute organ damage. Another 10 patients with chronic hypertension were taken as **control group**. BNP was measured in the blood at the time of admission based on the principle of competitive enzyme immunoassay.

Results:- There was no significant correlation between the patients' age (58.5±12) and BNP level (183.67±216.3) *(r = -0.17, P = 0.3).* There was no significant difference in BNP level between males (223.35±179.2) and females

(131.77±255.2) *(p = 0.2)* and it was significantly higher in H.E patients (324.33 ±233.16) than H.U patients (43±13.5) and control (8.13±5.8) groups with p-value of <0.001. There was no significant difference in BNP level between H.E patients with cardiac (313.33±179.6) and neurological involvement (313.67±273.5) (p= 0.8), *also*, there was no significant difference in BNP level between patients presented with ischemic stroke (248.75±171), hemorrhagic stroke (255±132) and hypertensive encephalopathy (970) (p= 0.3). Moreover, there was no significant correlation between BNP and systolic B.P, diastolic B.P, mean arterial pressure and pulse pressure in both studied patients and control groups (P>0.05 in all). Receiver operator characteristic (ROC) curve was calculated for the use of BNP level as a diagnostic marker. The area under curve (AUC) for BNP as a diagnostic marker was 0.96.

Conclusion:- During hypertensive crisis BNP blood level determination could have a role as a diagnostic tool for the screening of H.E and its evaluation is very useful in patients admitted with acute and rapid elevation of B.P to limit target organ damage.

Key words:- B-type natriuretic peptide; hypertensive emergency; hypertensive urgency; hypertensive crisis.

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Contents

List of Tables

List of Figures

List of Abbreviations

µl	*Microlitre*
ACE	*Angiotensin Converting Enzyme*
ACS	*Acute Coronary Syndrome*
ACTH	*Adrenocorticotropic Hormone*
AF	*Atrial Fibrillation*
Alb.	*Albumin*
ANG	*Angiotensin*
ANP	*Atrial Natriuretic Peptide*
ASCOT	*Anglo-Scandinavian Cardiac Outcome Trial*
AT	*Angiotensin receptor*
AUC	*Area Under The Curve*
AV	*Aortic valve*
AVP	*Arginine Vasopressin*
BNP	*B-Type Natriuretic Peptide or Brain Natriuretic Peptide*
BP	*Blood Pressure*
CAD	*Coronary Artery Disease*
cGMP	*Cyclic Guanosine Monophosphate*
CHF	*Congestive Heart Failure*
CI	*Cardiac Index*
CNP	*C-Type Natriuretic Peptide*
CO	*Cardiac Output*
Cr.	*Creatinine*
Cr.cl	*Creatinine Clearance*
CT	*Computed Tomography*
CVD	*Cerebro Vascular Disease*
D.M	*Diabetis Mellitus*
DBP	*Diastolic Blood Pressure*
DNP	*Dendroaspis Natriuretic Peptide*
E.R	*Emergency room*
ECG	*Electrocardiogram*
EDTA	*Ethylenediaminetetraacetic Acid*
EF	*Ejection fraction*
EIA	*Enzyme Immunoassay*
ESRD	*End-Stage Renal Disease*
ET-1	*Endothelin-1*
F	*Female*

FFA	*Free Fatty Acid*
fmol	*Femtomole*
GFR	*Glomerular Filtration Rate*
H.R	*Heart rate*
Hb	*Hemoglobin*
HE	*Hypertensive Emergency*
HEn	*Hypertensive Encephalopathy*
Hge.	*Hemorrhage*
HS	*Hemorrhagic Stroke*
HTN	*Hypertension*
HU	*Hypertensive Urgency*
ICH	*Intra Cranial Hemorrhage*
ICU	*Intensive Care Unit*
IL	*Interleukin*
INC	*Incorporation*
INR	*International normalized ratio*
IS	*Ischemic Stroke*
JNC	*The Joint National Committee*
K^+	*Potassium*
LBBB	*Left bundle branch block*
Lt.	*Left*
LV	*Left Ventricle*
LVEF	*Left Ventricular Ejection Fraction*
LVESWS	*LV End-Systolic Wall Stress*
LVH	*Left Ventricular Hypertrophy*
M	*Male*
MAP	*Mean Arterial Pressure*
MI	*Myocardial Infarction*
min.	*Minute*
ml	*Milliliter*
mmHg	*Millimeter Mercury*
MR	*Mitral regurge*
MRFIT	*The Multiple Risk Factor Intervention Trial*
MRI	*Magnetic Resonance Imaging*
mRNA	*Messenger RNA*
MVP	*Mitral valve prolapse*
Na^+	*Sodium*
NADPH	*Nicotinamide Adenine Dinucleotide Phosphate*
NEFAs	*Non-Esterified Fatty Acids*
NEP	*Neural Endopeptidase*

NF-B	*Nuclear Factor-B*
nm	*Nanometer*
NPR	*Natriuretic Peptide Receptor*
NPs	*Natriuretic Peptides*
NSR	*Normal sinus rhythm*
NT pro-BNP	*N-Terminal Pro-BNP*
O_2	*Oxygen*
PCWP	*Pulmonary Capillary Wedge Pressure*
pg	*Picogram*
PP	*Pulse Pressure*
PTCA	*Percutaneous Transluminal Coronary Angioplasty*
RAS	*Renin Angiotensin Aldosterone System*
RBBB	*Right bundle branch block*
Ren-2	*Renin-2*
ROC	*Receiver Operator Characteristic*
Rt.	*Right*
SA-HRP	*Streptavadine-Horseradish Peroxidase*
SBP	*Systolic Blood Pressure*
SD	*Standard Deviation*
SGOT	*serum glutamic oxaloacetic transaminase*
SGPT	*serum glutamic-pyruvic transaminase*
SNS	*Sympathetic Nervous System*
Temp.	*Temperature*
TGF-β	*Transforming Growth Factor Beta*
TLC	*Total leukocytic count*
TMB	*Thermo Scientific Pierce*
TNF-α	*Tumor Necrosis Factor Alpha*
TOD	*Target organ damage*
TR	*Tricuspid regurge*
TSH	*Thyroid stimulating hormone*
U.S	*United states*
VEGF	*Vascular Endothelial Growth Factor*
vs	*Versus*
WMA	*Wall motion abnormality*
α	*Alpha*
β	*Beta*

Introduction

Hypertensive crisis is characterized by a rapid elevation of blood pressure (BP) in patients both with known or unknown arterial hypertension[1].Although there is no blood pressure threshold to differentiate a crisis from a less urgent situation for the diagnosis of hypertensive emergency, most crises are associated with diastolic blood pressures ≥ 120 mm Hg. Moreover, the magnitude of BP elevation is probably less important than the rapidity of the increase.[2]

Hypertensive crisis includes hypertensive emergencies and urgencies. Hypertensive emergency is defined as severe hypertension with acute end-organ damage; the most important complications include ischemic stroke, encephalopathy, hemorrhagic stroke and myocardial ischemia. Hypertensive urgency, on the other hand, describes significantly elevated blood pressure but without evidence of acute end-organ damage.[3]

It is not so easy to make a quick screening between HE and HU, as it often requires sophisticated, complex and time consuming clinical, instrumental and diagnostic tests. The usual diagnostic process includes

brief focused neurological and cardiovascular examinations, ECG, chest x-ray, CT of the brain, urine analysis and creatinine evaluation. [4]

The natriuretic peptide family consists of three members: atrial natriuretic peptide, brain natriuretic peptide, and C-type natriuretic peptide. Atrial and brain natriuretic peptides possess similar effects, causing natriuresis, vasodilatation, and suppression of the renin-angiotensin-aldosterone system. C-type natriuretic peptide has been suggested to exert its predominant effect on the vasculature, eliciting vasodilatation and inhibiting the proliferation of vascular smooth muscle cells.[5]

Numerous studies have broadened our current knowledge of the regulation of natriuretic peptide gene expression, biosynthesis, and secretion, as well as structure of specific receptors. This has led to a better understanding of the renal, cardiovascular, and endocrine actions of natriuretic peptides in both normal and pathophysiological states, including hypertensive disease.[5]

B-type natriuretic peptide (BNP), with the inactive fragment N-Terminal pro-hormone brain natriuretic peptide (NT-proBNP), is a peptide synthesized by atrial and ventricular cardiomyocytes, with a potent

vasodilator, diuretic and natriuretic action; it decreases sympathetic outflow and inhibits vasopressin release. [6]

Aim of The Study

There are no enough data on the potential diagnostic and prognostic role of BNP detection in distinguishing between HE and HU. In the following study we will try to address the role of BNP in hypertension and how to use it to differentiate HE from HU to alleviate possible complications.

Natriuretic Peptides

Overview and History

The history of the research on the natriuretic peptides can be traced back to 1956 when early studies using the electron microscope showed that granules similar to those in endocrine glands were found in the cells of the atria.[7]

At that time, vasopressin and the renin–angiotensin–aldosterone system were known as regulators of natriuresis, but it was thought that there was another factor (called the 'third factor') which participates in natriuresis. It was also known from a clinical standpoint that natriuresis occurs following supraventricular attacks which suggested that this 'third factor' was linked to the heart .[8]

A major discovery and advancement in the identification of atrial natriuretic peptide was made by de Bold in 1981 who showed that intravenous injection of atrial myocardial extract causes a rapid and potent natriuretic response in rats.[9]