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ROLE OF HEPARIN BINDING PROTIEN (HBP) AZUROCIDIN CAP37 AND BRACHIAL ARTERY REACTIVITY AS PROGNISTIC TESTS IN CRITICALLY ILL PATIENTS WITH SEPSIS

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in Critical Care Medicine**

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Abstract

ROLE OF HEPARIN BINDING PROTEIN (HBP) AZUROCIDIN CAP37 AND BRACHIAL ARTERY REACTIVITY AS A PROGNOSTIC TESTS IN CRITICALLY ILL PATIENTS WITH SEPSIS**Introduction:**

Rapid detection of the presence as well as optimized treatment of severe sepsis and septic shock is crucial for successful outcome.

Heparin-binding protein (HBP), a potent inducer of increased vascular permeability, is a potentially useful biomarker for predicting outcome in severe sepsis patients. Ultrasound measurements of brachial artery reactivity in response to stagnant ischemia provide estimates of microvascular function and conduit artery endothelial function.

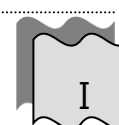
We hypothesized that brachial artery reactivity and HBP levels would independently predict severe sepsis occurrence and mortality.

Our Aim is to identify the role of both Heparin-binding protein (HBP) and brachial artery reactivity Compared to APACHE II and SOFA scores as predictors of morbidity and mortality in critically ill septic patients

Methods: An observational prospective controlled study of patients admitted in the Critical Care Department at Cairo University Egypt. Patients were classified into two groups GROUP I which included 38 patients : Sepsis (2 patients); Severe sepsis (20 patients) who had sepsis and target organ damage and Septic shock (16 patients) who had severe sepsis and developed inadequate tissue perfusion. Control group: GROUP II includes 10 critically ill patients who did not develop sepsis in their hospital clinical course. HBP Blood samples were collected at three time points during six days after admission. We measured brachial artery reactivity in 38 severe sepsis patients and in 10 control patients acute illness other than sepsis, Measurements were compared in severe sepsis patients versus control subjects and in survivors versus non-survivors. Multivariable analyses were also conducted.

Results: Significant difference was detected between Survivors and Non-survivors in max SOFA score, Baseline WBCs, WBCs at 48 and 96 h as well as Baseline HBP, HBP at 48h and 96 h, where the result were in non-survivors versus survivors respectively {5.9(4.8-6.6)}ng/ml vs {1.2(0.4-1.6)}ng/ml at baseline; { 6.5(4.8-7.5)}ng/ml vs {1.2(1.2-1.7)}ng/ml at 48 hours and lastly {6.0(4.5-6.6)}ng/ml vs {1.12(0.8-1.4)} ng/ml at 96 hours . (ROC) curve analysis for prediction of severe sepsis, septic shock using Baseline HBP, AUC:0.982 , $P < 0.0001$ with sensitivity 94.7% specificity 100%, cut-off level >1.9 ng/ml, (ROC) curve analysis for prediction of mortality using Baseline HBP level, (AUC) =0.99, P -value < 0.0001 , Sensitivity 91.6%, Specificity 100%, associated criterion >1.9 ng/ml. Highly significant difference exists between survivors and Non-survivors respectively in FMD, Baseline velocity, Hyperemic velocity, Velocity difference and Post-deflation RI. The results were in non-survivors versus survivors respectively for FMD% {2.3(1.9-2.8)} % vs {5.5(4.7-5.8)} %. Baseline velocity cm/cardiac cycle {12(9.7-14.3)} vs {20(17.6-22)}. Hyperemic velocity (cm/cardiac cycle) was {20.5(18-25)} vs {52.3(47.5-55)} and for Velocity difference (cm/cardiac cycle) {8.55(8-10)} vs {31.75(28.3-34)} And for Post-deflation RI { 0.78(0.72-0.81)} in Non-survivors vs {0.53(0.48-0.55)} Survivors . (ROC) curve analysis for prediction of severe sepsis/septic shock using:-FMD: (AUC) =0.97, P -value < 0.0001 , Sensitivity 94.7%, Specificity 100%, PPV = 100%, NPV = 83.3% and associated criterion ≤ 3.4 %, Hyperemic velocity (AUC) =1, P -value < 0.0001 , Sensitivity 100%, Specificity 100%, PPV = 100%, NPV = 100% associated criterion ≤ 39 (cm/card cycle). (ROC) curve analysis for prediction of mortality using: FMD, (AUC) =1, P -value < 0.0001 , Sensitivity 100%, Specificity 100%, PPV = 100%, NPV = 100% and associated criterion ≤ 3.4 %, Hyperemic velocity (AUC) =1, P -value < 0.0001 , Sensitivity 100%, Specificity 100%, PPV = 100%, NPV = 100% and associated criterion ≤ 39 cm/cardiac cycle. Kaplan-Meier survival analysis for patients with FMD < 3.4 % or > 3.4 %, p -value 0.046. Hyperemic velocity < 30 or > 30 cm/c cardiac cycle, p -value 0.046 and Velocity difference < 13 or > 13 cm/c cycle, p -value: 0.046.

Conclusions: Plasma HBP levels and brachial artery reactivity were significantly different in patients with severe sepsis or septic shock compared to non-septic ICU patients, and both tests can predict morbidity and mortality in critically ill septic patients. Comparison of the receiver-operating characteristic (ROC) curves for prediction of 28-mortality using the SOFA max, APACHE II score, HBP max, FMD and hyperemic velocity , there wasn't different between variable.



Contents

Introduction	1
Aim of The Work	5
Review of Literature	
• <i>Definition , diagnosis &Pathophysiology sepsis.</i>	6
• <i>Heparin-Binding Protein</i>	31
• <i>Ultrasound assessment of flow-mediated dilation and hyperemic velocity : a tutorial</i>	41
Patients & Methods	72
Results	78
Discussion	123
Summary	142
Conclusions	144
References	146
Arabic Summary	

List of Tables

Table No.	Title	Page
Table (1)	: The SOFA score	9
Table (2)	: Inflammatory mediators in sepsis	13
Table (3)	: Evidence of alterations in blood velocity and blood flow as a consequence of insonation angle	50
Table (4)	: Absolute difference and variability between manual and software evaluations of FMD determinants	65
Table (5)	: Difference in fmd and determinants using 3, 5, and 10 second data smoothing averages	67
Table (6)	: Demographic data of patients group G I and control G II	78
Table (7)	: Hemodynamic data of patients GI and control G II group at recruitment and end of follow up .	79
Table (8)	: Scoring system in of patients GI and control G II group at recruitment and end of follow up .	80
Table (9)	: Lab parameters in patients GI and control G II at baseline,48 and 96 hours	81
Table (10)	: ABG parameters in patients G1 and control groupG1 I at recruitment and end of follow up .	83
Table (11)	: Duplex parameters in patients GI and control G II group.	84
Table (12)	: Demogrpic data in comparison of patients GI and control G II group: categorical variables.	87
Table (13)	: Morbidity & mortality in comparison of cases GI and controls G II	88
Table (14)	: Demographic data of comparison of survivors and non survivors	89
Table (15)	: Source of infection in comparison between survivors and non-survivors	90
Table (16)	: Microbiology comparison between survivors and non-survivors	91
Table (17)	: Hemodynamic data comparison of survivors and non-survivors at recruitment and end of follow up .	92

Table (18)	:	ABG parameters in comparison of survivors and non-survivors at recruitment and end of follow up .	98
Table (19)	:	Lab parameters in comparison of survivors and non-survivors	94
Table (20)	:	Duplex parameters in comparison of survivors and non-survivors.	95
Table (21)	:	Scoring system in comparison of survivors and non-survivors at recruitment and end of follow up .	96
Table (22)	:	Morbidity and mortality in survivors and non-survivors	99
Table (23)	:	HBP as predictor of severe sepsis/septic shock	100
Table (24)	:	Prediction of severe sepsis/septic shock using duplex parameter.	102
Table (25)		Prediction of mortality using hbp level at various times	106
Table (26)		Prediction of mortality using duplex parameters	108
Table (27)		Prediction of mortality using variable parameters	112
Table (28)		Comparison of the receiver-operating characteristic (roc) curves for prediction of 28-mortality using the SOFAMAX, APACHE II SCORE, HBPMAX, FMD, or hyperemic velocity	115
Table (29)		This table shows trials similar to our article	124

List of Figures

Figure No.	Title	Page
Figure (1)	: PIRO	10
Figure (2)	: Potential outcomes of mediator release in sepsis	14
Figure (3)	: Complement activation in sepsis	18
Figure (4)	: The Response to Pathogens, Involving “Cross-Talk” among Many Immune Cells, Including Macrophages, Dendritic Cells, and CD4 T Cells.	29
Figure (5)	: The image quality of B-mode images using different frequency linear probes.	47
Figure (6)	: The determination of blood velocity and blood flow using different placements of the Doppler sample gate	58
Figure (7)	: The relationships between flow-mediated dilation (FMD) and different assessments of shear rate to be considered when normalizing FMD.	69
Figure (8)	: . Box plot showing HBP levels at various times in cases (GI) and controls(GII)	82
Figure (9)	: Box plot showing FMD in both study groups	85
Figure (10)	: Box plot showing baseline velocity, hyperemic velocity, and velocity difference in cases and controls	85
Figure (11)	: Box plot showing pre-occlusion and post-deflation RI in cases and controls	86
Figure (12)	: Mortality rate in both study groups	88
Figure (13)	: Box plot showing HBP level at various times in Survivors and Non-survivors	96

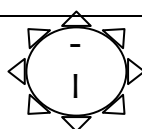
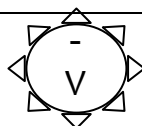


Figure (14)	:	Box plot showing FMD in Survivors and Non-survivors	97
Figure (15)	:	Box plot showing baseline velocity, hyperemic velocity, and velocity difference in Survivors and Non-survivors	97
Figure (16)	:	Box plot showing pre-occlusion and post-deflation RI in Survivors and Non-survivors	98
Figure (17)	:	Percentage of cases and controls among Survivors and Non-survivors.	99
Figure (18)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using baseline HBP level	100
Figure (19)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using HBP level at 48 h	101
Figure (20)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using HBP level at 96 h.	101
Figure (21)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using FMD	103
Figure (22)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using baseline velocity	103
Figure (23)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using hyperemic velocity	104
Figure (24)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using velocity difference	104
Figure (25)	:	Receiver-operating characteristic (ROC) curve for	105

		prediction of severe sepsis/septic shock using pre-occlusion RI	
Figure (26)	:	Receiver-operating characteristic (ROC) curve for prediction of severe sepsis/septic shock using post-deflation RI	105
Figure (27)	:	Receiver-operating characteristic (ROC) curve for prediction of mortality using baseline HBP level	106
Figure (28)	:	Receiver-operating characteristic (ROC) curve for prediction of mortality using HBP level at 48 h	107
Figure (29)	:	Receiver-operating characteristic (ROC) curve for prediction of mortality using HBP level at 96 h	107
Figure (30)		Receiver-operating characteristic (ROC) curve for prediction of mortality using FMD	109
Figure (31)		Receiver-operating characteristic (ROC) curve analysis for prediction of mortality using baseline velocity	109
Figure (32)		Receiver-operating characteristic (ROC) curve for prediction of mortality using hyperemic velocity	110
Figure (33)		Receiver-operating characteristic (ROC) curve for prediction of mortality using velocity difference	110
Figure (34)		Receiver-operating characteristic (ROC) curve for prediction of mortality using pre-occlusion RI	111
Figure (35)		Receiver-operating characteristic (ROC) curve for prediction of mortality using post-deflation RI	111

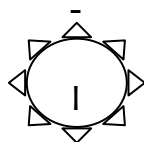
Figure (36)	Receiver-operating characteristic (ROC) curve for prediction of 28-mortality using the SOFAMax.	113
Figure (37)	Receiver-operating characteristic (ROC) curve for prediction of 28-mortality using the APACHE II score.	113
Figure (38)	Receiver-operating characteristic (ROC) curve for prediction of 28-mortality using the HBPmax.	114
Figure (39)	Comparison of the receiver-operating characteristic (ROC) curves for prediction of 28-mortality using the SOFAMax, APACHE II score, HBPmax, FMD, or hyperemic velocity	116
Figure (40)	Kaplan-Meier survival curves for patients with baseline HBP >3.4 or ≤ 3.4 ng/ml	117
Figure (41)	Kaplan-Meier survival curves for patients with HBP >3.8 or ≤ 3.8 ng/ml at 48 h	117
Figure (42)	Kaplan-Meier survival curves for patients with HBP >1.6 or ≤ 1.6 ng/ml at 96 h	118
Figure (43)	Kaplan-Meier survival curves for patients with pre-occlusion diameter ≤ 4 or >4 cm	118
Figure (44)	Kaplan-Meier survival curves for patients with post-deflation diameter ≤ 4.3 or >4.3	118
Figure (45)	Kaplan-Meier survival analysis for patients with FMD $<3.4\%$ or $\geq 3.4\%$	119

Figure (46)	Kaplan-Meier survival curves for patients with baseline velocity ≤ 16 or > 16 cm/cardiac cycle	119
Figure (47)	Kaplan-Meier survival curves for patients with hyperemic velocity ≤ 30 or > 30 cm/cardiac cycle	120
Figure (48)	Kaplan-Meier survival curves for patients with velocity difference ≤ 13 or > 13 cm/cardiac cycle	120
Figure (49)	Kaplan-Meier survival curves for patients with pre-occlusion peak velocity > 64 or ≤ 64 cm/cardiac cycle	120
Figure (50)	Kaplan-Meier survival curves for patients with post-deflation peak velocity > 64 or ≤ 64 cm/cardiac cycle.	121
Figure (51)	Kaplan-Meier survival curves for patients with pre-occlusion RI > 0.76 or ≤ 0.76 cm/cardiac cycle	121
Figure (52)	Kaplan-Meier survival curves for patients with post-deflation RI > 0.64 or ≤ 0.64 cm/cardiac cycle	122



List of Abbreviations

A-a gradient	:	Alveolar arterial gradient
ACTH	:	AdrenoCorticotrophic Hormone
ADP	:	Adenosine Diphosphate
ALI	:	Acute Lung Injury
ALB	:	Albumin
APACHE II	:	Acute Physiology and Chronic Health evaluation
APTT	:	Activated Partial thromboplastine time
ARDS	:	Acute respiratory distress syndrome
ATP	:	Adenosine Triphosphate
AUC	:	Area under the curve
C	:	Sound velocity
CAP37	:	Cataionic antimicrobial protein of 37
CAP	:	Community Acquired Pneumonia
CLP	:	Ceacal Ligation&Puncture
CNS	:	Central Nervous System
CRH	:	Corticotropine Releasing Hormone
CRP	:	C Reactive Protein
CT	:	Computed Tomography
CVC	:	Central Venous Catheter
CVP	:	Central Venous Pressure
CVS	:	Cerebrovascular stroke
DC	:	Dentritic cells
DIC	:	Disseminated Intravascular Coagulopathy



DM	:	Diabetes Mellitus
Dob	:	Dobutrex
DOP	:	Dopamine
DVT	:	Deep Venous Thrombosis
E Coli	:	Escherichia Coli
EPI	:	Epinephrine
eNOS	:	Endothelial nitric oxide synthetase
fd	:	Doppler shift
FDP	:	Fibrin Degradation Products
FFP	:	Fresh Frozen Plasma
FMD	:	Flow mediated dilatation
fMLP	:	Formyl-methyl-leucyl-phenylalanin
fo	:	Transmitted frequency
G.CSF	:	Granulocyte Colony Stimulating Factors
GNBs	:	Gram Negative Bacilli
HAP	:	Hospital Aquired Pneumonia
HBP	:	Heparin binding protein
Hb	:	Hemoglobin
HIV	:	Human Immunodeffiecincy Virus
HR	:	Heart rate
HTN	:	Hypertension
ICU	:	Intensive Care Unite
IL2	:	Interlukine 2
IL6	:	Interlukine 6
K	:	potassium

