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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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Talal hagag

Abstract

ROLE OF HEPARIN BINDING PROTIEN (HBP) AZUROCIDIN CAP37 AND BRACHIAL ARTERY REACTIVITY AS A PROGNISTIC 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 pateints : 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.

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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	:	Dentretic cells
DIC	:	Dissemenated 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	:	Transmited 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