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Review Article

STUDY ON IMPACT OF THE COPEPTIN IN THE DIAGNOSIS OF MALE PATIENTS WITH ACUTE CORONARY SYNDROME

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ABSTRACT

Back ground: Acute coronary syndrome is a potentially life-threatening condition that affects millions of individuals each year. The introduction of biomarkers has brought improvement for both diagnostic and management of cardiac patients.Timely diagnosis of acute coronary syndrome in the emergency department remains challenging ,because of its delayed increase in plasma in the early phase of myocardial infarction , there is proof that copeptin is possibly useful as a diagnostic and prognostic biomarker in various cardiovascular diseases. **Objective:** This study carried out to evaluate serum copeptin levels in patients with acute coronary syndrome and healthy persons and study the correlation of these levels as indicator for patients with risk factors. **Patients & Methods:** A total (58) referred male patients with acute coronary syndrome were included in this study with age range (23-75year) and also included (30) healthy persons served as control with age range (27-70year). Random blood sugar ,lipid profile (total cholesterol, triglyceride, High density lipoprotein cholesterol and low- density lipoprotein cholesterol), troponin I, creatine kinase-MB and copeptin were measured for acute coronary syndrome patients and control . **Results:** Serum copeptin and lipid profile were significant increased in acute coronary syndrome in comparison with control group, while the level of high density lipoprotein decreased in sick patients in comparison with control group. Negatively significant correlation was found between Ejection Fraction and serum copeptin in acute coronary syndrome patients. Positively significant correlation was found between copeptin, troponin , creatine kinase -MB.

Key words: Acute coronary syndrome, male patients, copeptin, lipid profile, troponin.

INTRODUCTION

Acute coronary syndrome is a potentially life-threatening condition that affects millions of individuals each year, despite declining rates of hospitalization for MI, the identification and prevention of ACS continues to be an important public health concern, over the past several years, Timely diagnosis of acute coronary syndrome (ACS) in the emergency department remains challenging [1]. Initial diagnostic testing for ACS begins with an Electrocardiography (ECG) , however, the sensitivity of the initial ECG for diagnosing acute myocardial infarction (AMI) has been reported to be as low as 60%, even when used in combination, history and physical examination, initial ECG, cannot reliably exclude ACS[2]**.** The introduction of biomarkers has brought improvement for both diagnostic and management of cardiac patients, there is also proof that copeptin is possibly useful as a diagnostic and prognostic biomarker in various cardiovascular diseases, it has been studied and proven for years that copeptin is a prognostic biomarker for myocardial infarction (MI),heart failure(HF), and acute decompensated HF[3][4][5]. Lastly, copeptin levels are available faster for analysis (1-5.5 hours from extraction) [6][7]. Unfortunately, troponins cannot differentiate between ischemic and non- ischemic causes of necrosis [6][8][9][10], troponins also have a delayed increase in plasma concentration (6-9 hours from onset of symptoms), which is why its sensitivity are low in the early phase of MI[6][11].

Previous study has been conducted on the usefulness of copeptin as a cardiac biomarker. it can be concluded that copeptin is a viable additional biomarker to diagnose AMI in early presentation without the need for a serial cardiac troponin [7].

PATIENTS & METHODS

This study was conducted at AL-Yarmouk Teaching Hospital and Ibn AL-Bitar Cardiac Center in cooperation with Department of Chemistry and Biochemistry/College of Medicine/Al Mustansiriyah University during the period from February 2018 until July 2018. A total (58) referred male's patients with ACS were included in this study with age range (23-75year) Data were collected by direct interviews with the patients by the researcher after obtaining their verbal consent to participate in the study,The diagnosis of ACS in every patient was done by a cardiologist based on clinical presentation and history of ischemic heart disease, which was confirmed by ECG, cardiac enzymes and quantitative cardiac Troponin The study included also (30) apparently healthy persons served as control with age range (27-70year). Physicians in a coronary care unit (CCU) of AL-Yarmouk Teaching Hospital and Ibn AL-Bitar Cardiac Center were doing the clinical examination of patients and control with Body Mass Index (BMI)and Blood Pressure(BP)[systolic blood pressure (SBP) and diastolic blood pressure(DBP)],pulse rate(PR) .The waist-hip and waist height ratios were determined by dividing the waist (cm)over the hip (cm) respectively and taking the cut-off ≥0.9.

Random blood sugar(R.B.S)[12] ,Lipid profile: total cholesterol(TC) [13], triglyceride(TG) [14], High density lipoprotein cholesterol(HDL)[15] ,low- density lipoprotein cholesterol (LDL) [16], and troponin I[17],Creatine kinase-MB ***(***CK-MB)[18] and copeptin were measured[19].

Exclusion criteria: Chronic kidney disease, Chronic liver disease, Systemic infections, Malignancy, diabetes, Advanced chronic obstructive pulmonary disease(COPD).

Statistical analysis: This analysis was carried on by using Excel 2016. Data were presented as percentage, mean, standard deviation (SD). To compare the significance of the difference in the mean values between patients and control; Student t-test and/or ANOVA were applied. Categorical variables are presented as n (%) and were compared with chi-square test. The correlation coefficient (r) test is used to describe the correlation between different parameters studied.

RESULTS

This study was done on 88 subjects (58 acute coronary syndrome patients and 30 healthy controls), all study subjects were males,

the mean ± SD of their age was 56.259±12.181, 51.8±12.516 respectively ,Table (1) summarizes the Baseline characteristics of study groups.

Table 1: Baseline characteristics of study groups (Mean ±SD)

Parameter	Study Group		P-value
	Patients(Mean ±SD)	Control (Mean ±SD)	
Age(year)	56.259±12.181	51.8±12.516	0.115
BMI(kg/m^2)	27.772±4.989	25.48±3.427	0.013
SBP(mmHg)	139.84±25.096	124.33±5.647	<0.0001
DBP(mmHg)	85.88± 14.91	75.97±6.473	<0.0001
PR (bpm)	80.328±14.836	74.9±7.743	<0.0001
Hypertension, n (%)	26 (44.8%)	3 (10%)	0.001
Dyslipidemia, n (%)	28 (48.3%)	3 (10%)	0.0003
Previous IHD [a], n (%)	24(41.3%)	0 (0%)	<0.0001
Family history, n (%)	23 (39.7%)	8 (26.7%)	0.227
Smoking ,n (%)	26 (44.8.%)	9 (36%)	0.178
Previous PCI [b], n (%)	15 (25.86%)	0 (0%)	0.002
Previous CABG [c], n (%)	4(6.9%)	0(0%)	0.141
Stroke, n (%)	2(3.4%)	0(0%)	0.0002
History of HF, n (%)	4(6.9%)	0(0%)	0.001

[a].IHD=ischemic heart disease;[b].PCI =percutaneous coronary intervention; [c]. CABG= coronary artery bypass graft.

Table (2) demonstrates that random blood sugar (R.B.S) and lipid profile levels regarding the TC, TG,LDL ,LDL/HDL and VLDL were significantly increased in ACS patients

Table 2: Random blood sugar and Lipid profile measurements in ACS patients and control groups (Mean± SD).

Parameter	Study Group		P-value
	Patients (Mean±SD)	Control (Mean±SD)	
R.B.S(mg/dl)	114.02±20.208	97.8±8.747	< 0.05
TC(mg/dl)	205.655 ±32.876	182.4±10.881	<0.0001
TG(mg/dl)	160.155± 50.579	131.113±27.263	0.0007
LDL(mg/dl)	133.852±28.656	109.777±10.352	<0.0001
HDL(mg/dl)	40.362± 7.661	46.967±7.421	0.0002
LDL/HDL	3.438±0.984	2. 472±0.399	< 0.05
VLDL(mg/dl)	31.603±9.005	26.223±5.453	0.0008

when compared to control while the levels of HDL were significantly decreased in ACS patients in comparison with control group.

Table (3) showed highly significant increase in concentrations of Creatine Kinase-MB (CK-MB), troponin and copeptin values in ACS patients in comparison with control group.

Table 3: CK-MB, troponin and Copeptin measurements in ACS patients and control groups (Mean± SD).

Parameters	Study Group		P-value
	Patients (Mean±SD)	Control (Mean±SD)	
Ck-MB(ng/ml)	16.036±24.339	5.101±1.525	0.001
Troponin (ng/ml)	4.822±5.583	0.24±0.155	<0.0001
Copeptin (ng/ml)	8.723±3.209	4.158.±1.922	<0.0001

A significant positive correlation is noted between copeptin and most parameters in patients with acute coronary syndrome (ACS) as shown in Table (4), among them a significant very strong positive correlation noted between copeptin and age, BMI, R.B.S, CK-MB, troponin, in addition there were a significant negative correlation between copeptin and Ejection Fraction (EF%).

Table 4: Correlation coefficient value (r) of Copeptin with all parameters in patients with acute coronary syndrome (ACS).

Parameters	Copeptin(ng/ml)	
	R	*P- value*
Ages(years)	0.293	0.027
BMI(kg/m^2)	0.322	0.015
SBP(mmHg)	0.4	0.002
DBP(mmHg)	0.315	0.017
EF%	-0.685	<0.05
R.B.S (mg/dl)	0.453	0.0004
TC(mg/dl)	0.059	0.661
TG(mg/dl)	0.065	0.633
LDL(mg/dl)	0.112	0.408
HDL(mg/dl)	0.045	0.741
LDL/HDL	0.132	0.327
VLDL(mg/dl)	0.058	0.668
Ck-MB(ng/ml)	0.604	<0.05
Troponin(ng/ml)	0.625	<0.05

DISCUSSION

This study shows that mean age group in patients more than control group despite not reaching level of statistical significance, which can be implicated by the emphasis on selection of age matched controls, the results was in agreement with other studies [20][21]. Elderly patients are more likely to have complications both from acute coronary syndrome and reperfusion therapy due to more vascular risk factors, frailty, and age related physiological changes. Furthermore, the expected mortality rate is higher [22]. Body mass index(BMI) reveals significant difference between patients in ACS and control group, this data came to conform with what has been reported previously on this parameter by several researchers[19][20][21].The study reveals that dyslipidemia was reported from history at presentation in about half of ACS group and this was statistically significant and consistent with other studies[21][23].

This study shows highly significant increase in TC, TG, LDL, LDL/HDL, VLDL and lower HDL in ACS group compared to control group, these results were in line with other researchers [20][21][24][25][26].Lipid profile levels play a serious role in cardiovascular risk assessment, the oxidation of low density lipoprotein cholesterol (LDL-C) is considered as the most important major factor for coronary artery disease which is the underlying cause of coronary artery disease[27][28].Also troponin and CK-MB are increased in ACS groups, which are consistent with recent studies [29][30]. Prolonged myocardial ischemia leads to an oxygen deficit and irreversible myocardial necrosis. A deficit in the delivery of blood to myocardial tissues, either due to increased demand or the presence of a ruptured coronary artery plaque causes myocardial ischemia which initiates a cascade of molecular and cellular events[31].The results of this study showed highly significant change in copeptin between ACS patients and control being higher for patients, these results were in accordance with other studies [19][20][29].These results are attributed to two hypotheses; first, the stress hypothesis where Copeptin/AVP is a substantial part of the endocrine stress response ,the second is the hemodynamic hypothesis where AMI results in hypotension leading to baroreceptor stimulation and finally secretion of Copeptin/AVP from the posterior pituitary gland[3][32][33].Other studies are in concordance with these results[34][35][36].Copeptin as a marker of acute stress, is excreted into circulation independent of necrosis of cardiac cells in cases of AMI[29][37]. This study showed that there are positive correlation between copeptin and age, BMI, SBP and DBP in ACS group , in addition to positive correlation with RBS in ACS ,these results were consistent with previous study[7].The results of the correlation study showed that there is significant negative correlation between copeptin and Ejection Fraction in ACS these results agreed with other researchers [29][35].Also this study revealed significant correlation between copeptin and all other biomarkers in ACS which was in agreement with other studies [19][38[39].

CONCLUSIONS

Our study revealed that Copeptin concentration is significantly higher in ACS patients in comparison with control, moreover, Copeptin rises at a time when other biomarkers namely the routinely used markers; cTns and CK-MB are still undetectable.

Copeptin can be affected by age and BMI.

Copeptin are positively correlated with all parameters, while negative correlation was found between Ejection Fraction (EF%) and serum copeptin in ACS patients

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