Evaluation of cTnI, cMYbPC3, CKMB and Reg3 beta in the patients with ACS

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Abstract

Background: In patients with (ACS), it is necessary to identify a sensitive and specific biomarker in the early diagnostic and prognostic evaluation. So, it is more essential for application of appropriate acute treatment and further management. The aim of the current study is to evaluate the levels of cTnI, cMYBP-C, CK-MB and Reg3β in the diagnosis of ACS. Materials and Methods: To find the levels of cTnI, cMYBP-C, CK-MB and Reg3β we measured patients who admitted to coronary care unit (CCU). 50 patients with ST- elevation myocardial infarction (STEMI), 50 patients with non-ST elevation myocardial infarction (NSTEMI), 50 patients with unstable angina (UA) and 50 persons as control healthy group. Both of cTnI, cMYBP-C and Reg3β was investigated by ELISA method to quantity their levels While, CK-MB was investigated by immune inhibition assay. Results: The level peak of cMYBP-C was higher in STEMI (84.28±5.15) then NSTEMI (54.04 ± 6.84) and less in UA (16.02 ± 0.73) when compared with control group (15.60 ± 0.71), while cTnI was higher in STEMI (8.31 ± 0.84) then NSTEMI (7.62 ± 0.91) and less in UA (0. 688 ± 0.03) when compared with control group (15.60 ± 0.71). On the other hand, the mean of CK-MB in STEMI was (102.54 ± 9.42) U/L, (99.48 ± 9.15) in NSTEMI, (15.28 ± 6.15) in UA and (14.26 ± 0.86) in control group. and finally, the mean of Reg3β in the same four groups was (178.20 ± 21.11) ng /L in STEMI, (174.88 ± 14.78) ng /L in NSTEMI, (84.92 ± 8.138) ng /L in UA and (60.80 ± 7.19) ng /L in control group. On the other hand, the level peak of Reg3β in STEMI was (178.20 ± 21.11) ng /L, (174.88 ± 14.78) ng /L in NSTEMI, (84.92 ± 8.138) ng /L in UA and (60.80 ± 7.19) ng /L in control group. Conclusion: Our finding showed that increase the level of cMYBP-C earlier than cTnI and CK-MB. Then it considers a good marker for diagnosis STEMI and NSTEMI. While the increase level of Reg3β related with the intensity of inflammation the cardiac muscle.

Keywords: Acute coronary syndrome, STEMI, NSTEMI, UA, c-MYBP-C, cTnI, Reg3β, Ck-MB.

1. Introduction

Acute coronary syndrome (ACS) refers to any group of symptoms attributed to sever obstruction of the coronary arteries. The most common symptoms prompting diagnosis of ACS is chest pain, often radiating to the left arm or angle of the jaw, pressure, nausea and sweating [1].This term includes ST- elevation myocardial infarction (STEMI) which is recognized by complete occlusion of the coronary artery, non – ST elevation myocardial infarction (NSTEMI) which is recognized by partial occlusion of the coronary artery, and unstable angina (UA) [2] ACS is associated with a significantly high mortality rate, with serious cardiovascular complications secondary to atherosclerosis due to various factors such as oxidative stress anomalies, chronic inflammation and increased risk to thrombosis [3]. Several factors are implicated to have a significant effect on increasing the risk of coronary artery disease including age, sex, family history, and ethnicity. These factors are considered as non-modifiable factors while there are other factors that can be modified which include Diabetes type 2, hypertension, increased levels of serum cholesterol, LDL-cholesterol and triglyceride, decreased level of HDL-cholesterol, stress, smoking,obesity and sedentary life style [4]. Ischemia is the first step in the initiation of MI which results from disproportion between oxygen supply and its demand. This ischemia can often be diagnosed from patient history and from specific ECG changes.

Both clinical and laboratory findings including cardiac biomarkers and ECG changes are essential for the proper diagnosis of ACS [5]. Troponins are composed of three regulatory proteins, cTnC, cTnI, and cTnT [6]. cTnI, and cTnT are expected to increase within 2 to 3 hours after starting chest pain in patients with ACS and their level will remain elevated for up to 10 days while their peak is observed between 12-48 [7].

Creatine kinase (CK) is a high –energy output regulator of phosphate that is used in contractile tissues. It also plays a more general role in shutting high –energy phosphate bonds through creatine phosphate from the production site of ATP in the mitochondria to the cytoplasm utilization site [8]. Cytoplasmic CK is a dimer, composed of both M and / or B subunits, that produce CK-MM, CK-MB and CK-BB iso- enzymes CK also has a dimeric mitochondrial shape consists of sarcomeric and non – sarcomeric subunits [9].CK-MB is both a sensitive and specific and myocardial infarction marker. It usually becomes abnormal between 3-4 hours after myocardial infarction event, peak 10 -24 hours and returns to normal within 72 hours [10].Cardiac myosin binding protein C3 is a sarcomeric regulatory protein that controls cardiac contractile function [11, 12]. It is expressed in both ventricles and atriums. It is a large molecule about (150 KDa) consists of 10 domains of phosphorylation (M) [13]. Adult human muscle there are three cMYBP-C isoforms

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fast skeletal, (cMYBPC1), slow skeletal (cMYBPC2) and cardiac (cMYBPC3) expressed by individual genes [14]. cMYBP-C3 has recently shown to be extensively proteolysis during AMI and may be released into circulation as an biomarker for MI [15]. Reg3β is a small protein composed only by a single C- lectin domain and a short N- terminal peptide, which derives its secretion with 16.5 KDa. A feature of Reg3β protein appears when a cleavage site for trypsin near the N- terminal proceeded by signal peptide [16]. Reg3β, acts as a chemokine in the heart by promoting macrophage recruitment to the ischemic heart. Loss of Reg3β results in inadequate macrophage recruitment to the injured heart after MI, which compromises its healing and clinical outcome [17] Thus, macrophages, a major target of Reg3β, play a continuum of roles in cardiac remodeling and repair post-MI [18].

2. Materials and Method

From February 2020 to September 2020, five millilitres of whole blood were collected from patients hospitalised to the coronary care unit (CCU) at the Ibn Al –Bitar centre for heart surgery in Baghdad. The current study included 200 people, 150 of whom had ACS and the other 50 were in the control group with age range (35-70 year) and were divided into three groups, 50 people who had been diagnosed with ST elevation myocardial infarction (STEMI), 50 people who had been diagnosed with non-ST elevation myocardial infarction (NSTEMI), and 50 people who had been diagnosed with unstable angina (UA). In addition, another 50 people were chosen to serve as a control group. Males made up 102 of the total 150 cases, while females made up 48, which is an anticipated result given that ACS is more frequent in men.

The diagnosis of ACS is based on chest pain history, ECG abnormalities, and cardiac troponin increase. This research excluded patients with cardiac failure, CABG, dilated cardiomyopathy, and pregnant women cTnI was estimated by quantitative sandwich enzyme immunoassay technique, using the kit supplied by monobind inc. While Serum creatine kinase MB was measured by immune inhibition method assay using kit supply by human kit.

cMyBp-C was measured by competitive Elisa immunoassay technique, using the kit that supplied by instructional manual company. Finally, Reg 3β was measured by sandwich Elisa immunoassay technique, using the kit that supplied by MyBiosource company.

3. Statistical Analysis

The data in our research were presented in (mean±SE). The SPSS software program version 23 was used to evaluate all the parameters in our research. The considered P – value was < 0.05 to be edge of the significant level. ANOVA test was the major statistical test that was performed to compare means of various groups.

4. Results

A total number of 200 individuals were involved in the current study, 150 of them had ACS while the other 50 represented the control group with comparable age and sex. Mean age group of patients group was 62.4 years compared to 64.2 years in the control group. Of the total 150 patients, 102 were males while 48 were females which an expected finding as ACS is more common in males.

The final data of our work has been expressed in the table below table (1), and figure (1),(2),(3), (4) which shows the average level of serum cTnI, ckMB, cMyBPc, Reg3β in the studied population. The mean serum level cTnI was statistically determined in the four groups and was 8.31 ± 0.84 ng / ml in STEMI and 7.62 ± 0.91 ng / ml in NSTEMI, 0.688 ± 0.03 ng / ml in UA and 0.646 ± 0.04 ng / ml in control group, While the mean of cMyBP-C in the same four groups was 54.28 ± 5.15 mmole /L in STEMI 84.04 ± 6.84 mmole /L in NSTEMI, 16.02 ± 0.73 mmole /L in UA and 15.60 ± 0. 71 mmole /L in control group. In CK-MB the mean of STEMI was 102.54 ± 9.42 U/L, 99.48 ± 9.15 in NSTEMI, 15.28 ± 6.15 in UA and 14.26 ± 0.86 in healthy control group. and finally the mean of Reg3β in the same four groups was 178.20 ± 21.11 ng /L in STEMI, 174.88 ± 14.78 ng /L in NSTEMI, 84.92 ± 8.138 ng /L in UA and 60.80 ± 7.19 ng /L in control group.

Table (1): Mean ± SE of cTnI, cMYBPC3, ckMB and Reg3β in four studied groups.

Groups	Mean±SE) (cTnI (ng / ml)	Mean±SE) (cMYBP-C mmole /L)	CK- MB U/ L (mean± SE)	Mean ± SE ofReg3β (ng/ L)
Control	0.646±0.04	15.60±0.71	102.54±9.42	178.20 ± 21.11
STEMI	8.31±0.84	84.28±5.15	99.48±9.15	174.88 ± 14.78
NSTEMI	7.62±0.91	54. 04±6.84	15.28±6.15	84.92 ± 8.138
UA	0. 688 ± 0.03	16.02 ± 0.73	14.26±0.86	60.80 ± 7.19
P – Value	0.0001	0.0001	0.0001	0.0001

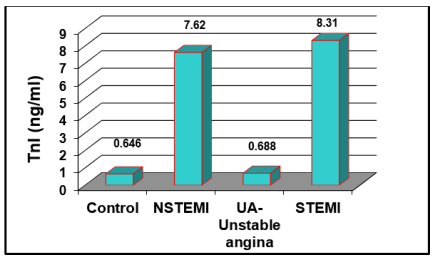

Figure 1. Comparison between difference groups in Tn

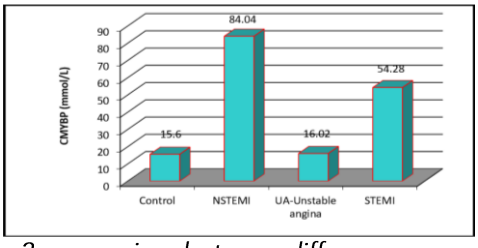

Figure 2: comparison between difference groups in c-MYBP-C

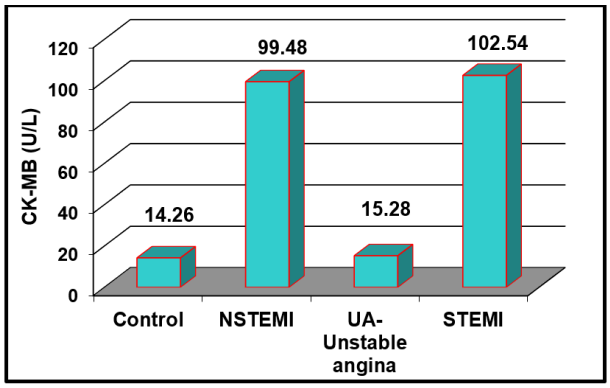

Figure (3): CK-MB activities in all studied groups.

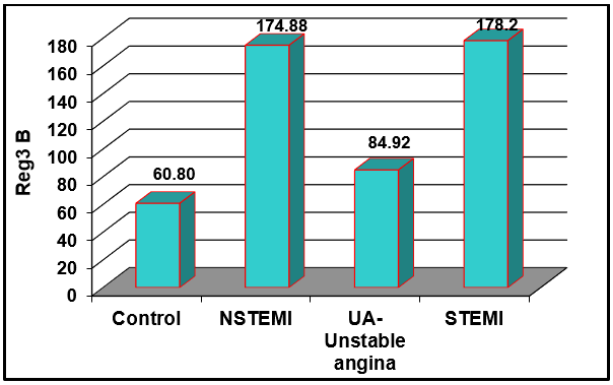

Figure (4): Reg3β level in all studied groups.

5. Discussion

As it was expected, the results of the current study have shown a significantly higher difference in mean serum cTnI between STEMI (8.31±0.84), NSTEMI (7.62 ± 0.91), UA (0. 688 ±0.03) respectively when compared to control group (0.646 ± 0.04) (P < 0.0001). Similarly, NSTEMI and STEMI have shown a higher significant differences compared to UA group (P < 0.0001) and STEMI has shown a significantly higher cTnI compared to NSTEMI. These results were comparable to the results of many similar studies which have discussed the role of cTnI as a diagnostic and prognostic indicator of ACS. Nearly identical results have been observed by Germán Cediel in respect to the diagnostic and prognostic value of cTnI in ACS [19]. The significant difference of cTnI between STEMI and NSTEMI has been detected by infrequent similar studies that confirmed the higher mean serum cTnI concentration in STEMI [20, 21]. Zachoval et al. [22] concluded that the initial elevated troponin levels were greatest in those with STEMI, then NSTEMI, and the lowest in those with UA that agree with present result.

At the same time both STEMI, NSTEMI groups have shown a high significant differences of serum cMyBP-C when compared to UA group (P < 0.0001). Similar results have been observed by [23, 24]and Giannitsis et al. [25] who detected a significantly high levels cMyBP-c and compared to troponin, it accumulates and disappear much faster than troponin. Many studies have suggested a superior role of cMyBP-c over troponin in diagnosis of ACS during the first hours after the onset of symptoms [26].The purpose of the measurement of the CK-MB in this study is to establish the diagnosis of MI in the suspected cases. According to Anova test, the results showed significant difference among all studied groups. When LSD test was performed, the results showed a significant elevation between STEMI and control group (P< 0.05), NSTEMI and control group (P< 0.05), whereas no significant between UA and control group (P > 0.05). Also, there were no significant differences between STEMI and NSTEMI (P> 0.05),while both of them have shown a significant differences when compared to UA group (P < 0.01).Ck-MB is very affected with infarction size,some studies approved this condition such as Liosis et al. [27] and Reinhardt et al. [28] They found repeated CK-MB testing for STEMI patients can be used to assess the peak value and estimate the infarct size for this group and show prognostic benefit for repeat marker sampling among NSTEMI patients as well [29] Although troponin is currently the recommended diagnostic marker for MI. Repeated measurement of CK-MB may be preferable for further risk stratification after diagnosis, because CK-MB levels are more prone to re- infarction diagnosis and can be processed at a lower price when comparison with troponin [4].

In respect to Reg3β, as it a potential biomarker of myocardial injury, there were a significant differences between STEMI,NSTEMI, UA respectively as compared to control group (P< 0.05).The increase level of Reg 3β STEMI,NSTEMI is higher than the patients with UA patients this is may be caused by extent of cell necrotic region is higher in STEMI, NSTEMI than UA.Thus, the inflammatory process initiate faster to release Reg 3β in these groups(STEMI and NSTEMI). Also, unstable angina occurs when either poor blood flow through the coronary vessels of the myocardium or partial obstruction of the coronaries that reverse in MI (NSTEMI, STEMI) in which a thrombus occurs, the decrease level of Reg3β in UA patients probably because of inhibition of many cellular processes in situation of which play very important role in cardiac healing such as inhibition of release Reg3β from macrophage and from damage area because there is no thrombus in the coronary arteries.

6. Conclusion

Although the increased level in cTnI in patients with STEMI then NSTEMI and not increase in patients with UA when compared with control group this is suggested a clear indication on the role of cTnI that used as an early biochemical marker in the diagnosis of ACS, but this study approved that cMYBP-C is significantly increased in patients with STEMI and NSTEMI and could be more preferred marker over cTnI in the early diagnosis of STEMI and NSTEMI. Also, cTnI can be used to distinguish between NSTEMI and UA in diagnosis. While CK-MB is significantly increased in both of STEMI, NSTEMI groups and this may help to diagnose re- infarction of two type of MI STEMI, NSTEMI.

On the other hand, the high level of serum Reg 3β, in STEMI then NSTEMI when compared to control group while non-significant in UA, is consider as a novel biomarker for determined the intensity of inflammation during ischemia and give more prognostic information for ACS.

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