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ORIGINAL ARTICLE

Association of Increased Oncostatin M with Adverse Left Ventricular Remodeling in Patients with Myocardial Infarction

ADNAN RIAZ[1], SABEEN KHALID[2], AMNA IHSAN[3], ANEELA SHABBIR[4], AHMAD ASHAR GHUMAN[5]
[1]*Assistant Professor of Biochemistry, Institute: Islam Medical College Sialkot*
[2]*Assistant professor, Department of biochemistry, M. Islam medical college Gujranwala*
[3]*Assistant professor Biochemistry, PhD scholar King Edward Medical University Lahore*
[4]*Assistant Professor Biochemistry, Foundation University Islamabad*
[5]*Associate Professor, Department of Biochemistry, Sialkot Medical College, Sialkot*
Corresponding author: Adnan Riaz, Email: dradnanriaz@yahoo.com, Cell: 03006103795

ABSTRACT

Background: Myocardial infarction is the leading cause of death worldwide. Patients suffering from myocardial infarction with a ST-elevated segment termed as STEMI experience high risk of death and these patients report recurrent attacks even more as compared to other MI patients.

Objective: The goal of this study was to check that either oncostatin M (OSM) can be used as a biomarker for the evaluation of myocardial infarction

Study design: This control-experimental study was conducted in Biochemistry department of the Islam Medical College, Sialkot.

Materials and methods: The study included 35 STEMI patients admitted in hospital, their oncostatin M level after 24 h of the onset of disease was calculated. The oncostatin M level after 6 months was later on analyzed. Electrocardiography was performed for all patients. The serum level was studied properly to look for level of biomarkers. The review board and ethical committee of the hospital approved the study.

Results: OSM level was increased after 24h of the onset of the disease. There was reduction in the level of OSM when measured after 6 months but still the levels suggested that OSM was detectable in the serum and can be used as a biomarker for myocardial infarction.

Conclusion: High levels of OSM in the serum after 24h can be attributed to its link with development of adverse LV remodeling among patients suffering from myocardial infarction. The OSM levels were decreased eventually but it was still high even after 6 months of the onset.

Keywords: CAD, oncostatin M, myocardial infarction, STEMI

INTRODUCTION

Myocardial infarction is the leading cause of death worldwide. Patients suffering from myocardial infarction with a ST-elevated segment termed as STEMI experience high risk of death and these patients report recurrent attacks even more as compared to other MI patients[1]. STEMI ultimately leads to heart failure and death. Even if there are number of modern techniques used as therapy to treat STEMI patients, Post-infarction complications like heart failure poses serious harm to patient's health[2]. In case of 20% of the cases such condition lead to readmission in the hospital[3]. The pathophysiological mechanism in case of adverse myocardial remodeling is the expansion of the infarct. The level of infarct expansion produced depends upon multiple factors like stress that was produced in the ventricular walls, size of infarction and the abnormal myocardial healing[3-4]. For the resolution of systemic and local inflammation, cytokines belonging to IL6 family play a very significant role. Oncostatin M is also a pleiotropic cytokine that is produced by T cells, dendritic cells and monocytes[5]. Oncostatin M is known to be one of the main factors that is involved in development of cardiovascular disorders[6]. As oncostatin M is responsible for proliferation, inflammation and other cellular differentiation processes. It was found that Oncostatin M is elevated among patients suffering from acute coronary stenosis. By causing autophagy and potential dedifferentiation of cardio myocytes, OSM is known to promote post-infarct myocardial healing[7-8]. The exact role of OSM in myocardial events became controversial when it became evident that it can have both harmful or healing effect depending on either the degree of disease is acute or mild. At present there is no data that shows exact OSM values in case of post infarct-remodeling in the left ventricle. There is no literature that can make a link of OSM being a biomarker for myocardial infarction or any heart injury[9]. There is some literature present but the studies are carried out on animals so it cannot be used for clinics[10]. Thus it was needed to find the OSM concentration so that it can be used as a biomarker for the early prognosis and treatment of myocardial infarction. In that case early and effective evaluation of the prediction and possibility of left ventricular remodeling could also be made.

MATERIALS AND METHODS

A total of 35 patients that visited tertiary care center during the course of one year were selected for the study. All these patients were admitted in the hospital and passed the first 24 h of the onset of the disease, fulfilled the inclusion criteria, the remaining patients were excluded from the study. Patients that had chronic LV dysfunction were excluded from the study. Those patients that were older than 75 years, or those who refused to participate in the study were also excluded. Protocol of study was approved by ethical committee. Written permission was taken from the patients. Echocardiography was carried out for all the patients after 24h of the onset of disease and after 6 months. Serum biomarker levels were evaluated, the blood samples of patients were taken and stored at -40°C until next use, then the levels were measured by using multiplex immunoassay with a high quality FLEXMAP 3D System. Statistical analysis was also carried out by making use of STATISTICA 10.0 software. P values were calculated and a p value less than 0.05 was considered as significant.

RESULTS

The study was carried out to find the level of M oncostatin and its effect on ventricular remodeling in patients suffering from myocardial infarction. The study was carried out in two groups, first group contained patients with STEMI (myocardial infarction with ST elevated segment**)** and group 2 had patients with acute CAD condition. The clinical features of the patients are listed in table no.1. The average age of the patients in STEMI group and in CAD group was 60± 9.4 and 61±7.4 years respectively. The percentage of patients suffering from hypertension diabetes mellitus and dyslipidemia is described in table no.1.

The correlation between the level of oncostatin M and different markers of myocardial infarction was carried out after 24 hours of onset of disease and after 6 months, electrocardiography patterns showed that only oncostatin M level was raised in the serum even after 6 months of onset of the disease all other factors including ΔESV (increased end systolic volume), Troponin µg/L

,Nt-pro BNP ng/L, CK-MB mg/L were reduced . The values are shown in table no.2. The serum level of these patients for all these biomarkers was analyzed. Univariate and multivariate analysis was carried out the results are shown in table no.3. P values were calculated and the results were statistically significant.

Table 1: Clinical features of patients suffering from STEMI (myocardial infarction with ST elevated segment) and acute CAD (coronary artery disease)

Features	STEMI patients n=35	Acute CAD patients n=40	P value
Average age	60± 9.4	61 ±7.4	0.005
Gender male (%)	73%	61%	0.003
Hypertension %	67%	26%	0.00
Diabetes mellitus %	22%	31%	0.001
Dyslipidemia %	71%	60%	0.001

Table 2: Correlation between oncostatin M and markers of myocardial infarction

Bio Markers	Serum concentration of biomarkers at the time of admission (24h)	Serum concentration of biomarkers after 6 months of STEMI	CAD patients n=40	p-value
OSM (oncostatin M) ng/L	41	21.12	4.91	0.001
ΔESV (increased end systolic volume)	1265.2	2.1	0.01	0.021
Troponin µg/L	140	0.09	1.3	0.001
Nt-pro BNP ng/L	1231.3	212	211	0.005
CK-MB mg/L	245.1	0.09	2.31	0.005

Table 3: Factors negatively effecting acute myocardial infarction

Factors	Univariable analysis			Multivariate analysis		
	OR	95% CI	P value	OR	95% CI	P value
Age	0.879	0.901-0.906	0.000	0.231	0.490-0.562	0.4261
Gender	1.000	1.341-1.445	1.000	0.990	0.213-0.344	0.002
Smoking	0.905	0.331-0.423	0.120	1.000	0.110-0.0012	0.001
BMI	0.782	0.123-0.273	0.000	1.120	1.321-3.62	0.005
ESV	0.046	0.789-0.645	0.001	0.999	0.333-0.989	0.000
LVEF	1.311	0.9030-0.997	0.002	1.342	0.990-0.998	0.110

The parameters that increased chances of left ventricular adverse remodeling were analyzed in both groups. It was found that the in case of 81% members of group 1 vascular lesion coronary arteries was causing left ventricular adverse remodeling as compared to group 2 where the percentage was 41%.

Table 4: Parameters that lead to left ventricular adverse remodeling

Parameters	Group 1 (n=35)	Group 2 (n=40)	P value
Pre-infarction angina %	41%	40%	0.151
Complete revascularization %	64%	57%	0.003
Vascular lesion coronary arteries %	81%	41%	0.005
Angina pectoris %	20%	23%	0.001
Thrombolysis and percutaneous coronary intervention %	59%	51%	0.000

DISCUSSION

This study has demonstrated that there is an increased level of oncostatin M at the early stage and even after 6 months of onset of myocardial infarction in the serum of patients, which lead to the development of adverse LV remodeling in 6 months after the onset of disease. The commonly used biomarkers of heart failure and myocardial infarction are ΔESV (increased end systolic volume), Troponin, Nt-pro BNP and CK-MB. Multiplex immunoassay was used for finding the serum level of these biomarkers. All the patients came for follow-up after 6 months of the disease onset. The values of Oncostatin M were in correlation to these biomarkers in the electrocardiograms. The clinical features of the patients were studied by taking data from the hospital and it was found that 67% STEMI patients suffered from hypertension as compared to CAD patients (26). The biomarkers that are commonly used for the myocardial infarction analysis were examined along with OSM, at first the level of OSM was high after the onset of the disease but after 6 months of the disease still the serum level of OSM was high as compared to other biomarkers whose level fell significantly after 6 months which makes OSM an effective marker for assessment of myocardial infarction. As per study there are multiple important roles of oncostatin M as it regulates hematopoiesis, inflammation and apoptosis[11-12]. There was a significant correlation found between the levels of these biomarkers and OSM in case of myocardial injury. The correlation between the level of oncostatin M and different markers of myocardial infarction was carried out after 24 hours of onset of disease and after 6 months, electrocardiography patterns showed that only oncostatin M level was raised in the serum even after six months of onset of the disease. While the remaining biomarkers showed reduced serum level after six months. Studies have shown that the regeneration of tissues and mesenchymal transition of stem cells is also regulated by oncostatin M[13-14]. As per literature there is an elevated level of OSM in the patients of coronary artery disease, atrial fibrillation and hypertension[15]. The OSM may be secreted by the macrophages present in the atherosclerosis plaques leading to acute atherosclerosis and ultimate failure of vascular endothelium[16-17]. The univariate and multivariate analysis was also carried out, p values were calculated and plotted in table no.3. Previously studies have shown that there is some involvement of OSM in the remodeling of heart but it was under study. Recent studies have demonstrated that the high levels of OSM cause the healing of myocardium leading to effectively treating cardiac fibrosis[18-19]. But these findings were found in mice where follow-up duration was not long. In case of CAD and STEMI the factors that led to left ventricular adverse remodeling were analyzed and it was found that in majority of the cases vascular lesion coronary artery is the condition that lead to left ventricular remodeling in case of STEMI patients. Another study showed that OSM at first cause healing of myocardium by incomplete de-differentiation of cardio myocytes but it also has adverse effect as the extensive and prolong cardio myocytes de-differentiation cause ventricular dilation leading to heart failure and death of the patient[20-21]. In our studies it was found that OSM levels were quite high after the 24h of disease onset which led to adverse effects in the long run. The level of other heart failure biomarkers was reduced after 6 months of treatment but the OSM levels were still elevated which shows that OSM can be used in future by scientists as biomarker of myocardial infarction. Here in this study it was found that as compared to CK-MB, OSM was much more effective biomarker for the LV remodeling. However, if it can be used in combination with other biomarkers it will have diverse and more effective results. There are certain limitations of this study, the sample size of patients was quite less. If there was a larger cohort of STEMI participants the study could be more clear. The sample was taken from a single hospital, if sample was taken from many different hospitals then diverse and more precise results could be made.

CONCLUSION

The patients suffering from STEMI had high levels of oncostatin M (OSM) in the serum after 24h of onset of the disease. The OSM levels was decreasing eventually but it was still high even after 6

months of the onset. OSM level correlates with the LV, ESV level and it can be used as a biomarker for the adverse left ventricular remodeling and it can improve the efficiency to diagnose STEMI patients.

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