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QTc Interval and Oxidative Stress Markers Variation in Acute Myocardial Infarction

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Original Research Article

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Abstract: Stress is common in day-to-day life and it affects many physiological functions of the body, mainly the cardiovascular system, may precipitate acute myocardial infarction (AMI), ventricular tachycardia and ventricular fibrillation. The present study was carried out to evaluate carbonyl stress (protein carbonyl), lipid profile and malondialdehyde (MDA) levels in AMI patients compared with healthy controls. Protein carbonyl is commonly used biomarker of oxidative stress; it is irreversible modification that develops when reactive aldehydes or ketones are added to amino acid residues. Samples were collected from 25 Acute myocardial infarction patients, 25healthy age and sex matched subjects were selected as control. The ECG results were evaluated for different parameters like heart rate, QRS complex, QTc intervals. Biochemical analysis like Lipid Profile, Protein carbonyl assay and serum MDA were done by using different standard methods Heart rate, SBP and DBP was more in AMI patients. Mean values of triglycerides levels, LDL Cholesterol levels were increased and HDL Cholesterol levels were decreased in the study group. There was statistically significant increase in malondialdehyde concentration and Carbonyl protein levels in AMI. To conclude increased QTc interval, elevated MDA and carbonyl protein in serum along with lipid profile are essential diagnostic tools for AMI. An elevated protein carbonyl (PC) level appears for a long period when compared with other parameters. Measuring protein carbonyl levels as biomarkers of oxidative stress has some advantages in comparison with the measurement of other oxidation products because of relative early formation and relative stability of carbonylated proteins.

Keywords: Acute myocardial infarction (AMI), Malondialdehyde (MDA), Reactive Oxygen Species (ROS).

INTRODUCTION

Acute myocardial infarction (AMI) occurs when there is an imbalance between supply and demand for oxygen in the heart muscle (myocardium) resulting in injury to and eventual death of muscle cells. Various risk factors for acute myocardial infarction are elevated like serum cholesterol, diabetes, and hypertension. Stress is common in day-to-day life and it affects many physiological functions of the body, mainly the cardiovascular system. Mental and physical stress is widely renowned as playing an important role in ventricular arrhythmias and sudden cardiac death. In fact, mental and physical stress can cause ischemia, and ischemia may precipitate ventricular tachycardia and ventricular fibrillation [1].

Electrocardiographic (ECG) QT intervals, as well as heart rate variability (HRV), blood pressure and heart rate, have been considered as a biomarker of the development of ventricular arrhythmia or of the susceptibility to sudden death, because QT intervals represent the duration between ventricular depolarization and subsequent repolarization. ECG is a commonly used test for cardiovascular studies [2, 3].

AMI is a clinical model of oxidative stress by ischemia reperfusion. The disturbance in the normal redox status of tissues cause toxic effects by production of peroxides and free radicals damages all cellular components [4]. Lipids and Proteins are the main targets for reactive oxygen species (ROS), alters the primary to quaternary structures. Increased ROS generation by vascular and inflammatory cells occurs in cardiovascular disease (CVD), and also elevated levels of oxidative biomarkers such as protein carbonyls (PC) and lipid peroxidation markers (MDA) [5].

Protein carbonyl is commonly used biomarker of oxidative stress; it is irreversible modification that develops when reactive aldehydes or ketones are added to amino acid residues. PC is generated by oxidative modification of peptide by alpha amidation pathway or oxidation of glutamyl side chains that leads to formation of a peptide in which the N-terminal amino acid is blocked by alpha keto acyl derivatives. Besides this, protein carbonyl may also be formed by reactions with aldehydes like Malondialdehyde (produced during lipid peroxidation) or with reactive carbonyl derivatives generated due to oxidation of reducing sugars or reaction of oxidized product with lysine residues of proteins[6]. The present study was carried out to evaluate carbonyl stress in AMI and compare protein carbonyl with standard laboratory lipid profile and Malondialdehyde (MDA).

MATERIALS AND METHODS

Study was conducted in the Department of Biochemistry, Rajah Muthiah Medical College Hospital, Chidambaram were included after taking informed consent from the patients. Serum samples collected from twenty five acute myocardial infarction patients who presented with symptoms of chest pain, epigastic pain or arm discomfort, breathlessness, nausea, and vomiting were included in the study. Patients having history of diabetes and thyroid dysfunction were excluded in the study. Screening with fasting blood sugar was performed and abnormal were excluded from the study. Twenty five healthy, age and sex matched subjects were selected as control. The ECG results were evaluated for different parameters like heart rate, PR interval, QRS complex, QT interval, QTc intervals.

Biochemical analysis like Fasting blood samples were collected in tubes and centrifuged at 2000×g for 10 min. Samples were analyzed for Fasting blood glucose by routine GOD-POD method, Lipid Profile (Total Cholesterol by CHOD-PAP, Triglycerides by Trinder, HDL by HDL-Precipitation & LDL by Direct method) using ERBA Chem – 5V2 semi auto analyzer, Protein carbonyl assay by spectrophotometric DNPH method [7] and serum malondialdehyde (MDA) by thiobarbituric acid reactive substance (TBARS) method.

STATISTICAL ANALYSIS

All results were shown as mean ± SD. The results were evaluated using Student's t-test. P-value <0.001 was considered statistically significant. Statistical analysis was performed using SPSS software

RESULTS

Table-1: **Mean ± SD of BP & ECG in Controls and AMI patients (**n=25)

Measurements	Controls	AMI patients	P value*
Heart rate (bpm)	74.88 ± 3.27	81.88 ± 3.72	0.001
Systolic BP (mmHg)	118 ± 3.74	122.9 ± 2.38	0.001
Diastolic BP(mmHg)	79.48 ± 2.485	82.24± 2.185	0.01
PR interval(sec)	0.152 ± 0.012	0.139 ± 0.010	0.001
QRS interval(sec)	0.080 ± 0.000	0.07 ± 0.004	0.001
QT(sec)	0.345 ± 0.013	0.340 ± 0.017	0.285
QTc(sec)	0.385±0.009	0.4±0.011	0.01

Date are expressed as mean ±SD, p<0.001 was considered statistically significant.

Table-2: Mean ± SD of lipid profile comparison in Controls and AMI patients

Parameters	Controls	AMI patients
Serum Cholesterol (mg/dl)	159.8±19.54	186.6±23.94*
Serum TG(mg/dl)	145.1±31.75	170.8±20.8*
HDL cholesterol (mg/dl)	40.2 ±2.784	37.76±4.013
LDL cholesterol(mg/dl)	102.1±14.26	133±19.79*

Date are expressed as mean ±SD, * p<0.001 was considered statistically significant, n=25

Table-3: Mean ± S.D of oxidative stress markers in Controls & AMI patients

Parameters	Controls	AMI patients
Malondialdehyde (µ mol/L)	2.63±0.739	9.89± 0.892 *
Carbonyl protein (n mol/dl)	13.99±1.949	22.25±2.493*

Date are expressed as mean ±SD, * p <0.001 was considered statistically significant, n=25

DISCUSSIONS

Heart rate (81.88 ± 3.72), Systolic BP (122.9 ± 2.38) and diastolic BP (82.24± 2.185) was more in AMI patients, when compared to that of controls (74.88 ± 3.27), (118 ± 3.74) and (79.48 ± 2.485) respectively and it was statistically significant (Table.1). The

increase in heart rate could be due to activation of sympathetic nervous system, vagal withdrawal because of stress. Increased heart rate is associated with increased mortality rates.

PR interval (0.139 ± 0.010) was shortened in AMI, when compared to that of controls (0.152 ± 0.012) (Table 1) and this was statistically significant. Stress could lead to augmentation of sympathetic system, catecholamine release which can lead to increase in the velocity of conduction in atria.

QRS interval (0.07 ± 0.004) was shortened when compared to that of controls (0.080 ± 0.001) with a difference of 0.01sec, and this difference was statistically significant (Table 1). Stress influences on intra ventricular conduction time by changing autonomic balance, which can lead to reduced QRS duration.

There was no much difference in duration of QT interval (0.340 ± 0.017) in MI when compared to that of rest (0.345 ± 0.013), and it was statistically not significant. But QTc interval (0.4±0.011) was slightly high in MI when compared to that of control (0.385±0.009) and it was statistically significant. (Table 2) Similar findings were reported by Ahnve S. Myocardial infarction (MI) could lead to autonomic nervous system (ANS) imbalance, adrenergic release, increased sympathetic tone, which can lead to ventricular depolarization heterogeneity leading to prolonged QTc interval [8].

Serum lipid profile in both control and in acute myocardial infarction patients groups is illustrated in (Table 2). In AMI patients with the mean values of cholesterol (186.6±23.94), triglycerides (170.8±20.8) levels were increased, when compared with control group of cholesterol levels (159.8±19.54) and triglycerides levels (145.1±31.75). Elevated levels of triglycerides after AMI may be due to increased fatty acids and impaired removal of VLDL from the circulation. [6]

LDL Cholesterol (133±19.79) levels were increased and HDL Cholesterol (37.76±4.013) were decreased in the study group, when compared with control group of LDL-Cholesterol (102.1±14.26) and HDL Cholesterol (40.2 ±2.784) (Table 2). Elevated levels of total cholesterol increases LDL levels as it carries most of the cholesterol. Reduced HDL cholesterol is shown to be associated with higher prevalence and incidence of coronary artery diseases. Several studies have supported that the ratio of LDL cholesterol & HDL cholesterol shows the atherosclerotic injuries of the wall of the vessels [9, 10].

Table 3 shows the relationship between Malondialdehyde (MDA) and Carbonyl protein content in AMI subjects with control. The table depicts significant increase in malondialdehyde conc. (9.89 ± 0.892) in AMI as compared with control (2.63±0.739). Lipid oxidation gives rise to a number of secondary products. Malondialdehyde (MDA) is the principal and most studied product of polyunsaturated fatty acid peroxidation. This aldehyde is a highly toxic molecule and should be considered as more than just a marker of lipid peroxidation. Its interaction with DNA and proteins has often been referred to as potentially mutagenic and thermogenic [11]. Carbonyl protein in AMI (22.25±2.493) when compared with control (13.99±1.949) significantly increased. Modification of proteins and production of carbonyl derivatives are the effects of oxidative stress on proteins. Carbonyl protein accumulation is generally assigned not only to oxidative stress but also to disease derived protein dysfunction [12].

CONCLUSION

Myocardial infarction is associated with oxidative damage which involved in molecular and cellular damage, which exposes protein to ROS leading to proteolysis and leads to elevation of protein carbonyl levels. Protein carbonyl content is a marker of protein oxidation, elevated PC levels appears for a long period when compared with other parameters. When PC levels are high along with altered lipid and cardiac profile levels in MI, it is an important diagnostic maker and also gives an idea of prognosis.

To conclude increased QTc interval, elevated MDA and carbonyl protein in serum along with lipid profile are some of the important diagnostic tools for acute myocardial infarction.

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