Indian Journal of Basic and Applied Medical Research; December 2017: Vol.-7, Issue- 1, P. 658 - 662

Original research article:

Free radical levels in acute myocardial infarction patients: a case control study

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Abstract:

Introduction- Acute Myocardial infarction (AMI) is a major cause of morbidity and mortality. Free radicals have been implicated among other causative factors of atherosclerosis and AMI. Malondialdehyde, an indicator of free radical induced damage, may be a biomarker of AMI.

Methods- Serum MDA was assayed in 64 AMI patients and 59 healthy conrols.

Observations - MDA levels were significantly greater in cases compared to controls.

Conclusions- AMI may be related to raise of MDA levels in serum. MDA may be considered as a useful biomarker of free radical status in AMI.

Keywords- Acute Myocardial infarction, malondialdehyde

Introduction:

Acute Myocardial infarction (AMI) is a major cause of morbidity and mortality worldwide (1). While the death rates have been declining for the past 3 decades in the West, these rates are progressively rising in India. The prevalence of known risk factors for coronary artery disease including central obesity, diabetes, hypertension and dyslipidemia is increasing. The co-existence of these risk factors, which are the constituents of the ubiquitous 'metabolic syndrome', confers a magnified risk that is multiplicative rather than additive. The predisposition to accelerated atherosclerosis seems to have a genetic component but is being compounded by changing lifestyles, dietary and cultural preferences, and sub-optimal heath care (2). Factors that predispose to atherosclerosis and therefore include, among several other agents, interplay between free radicals and antioxidants. Over the past 50 years, it has become clear that the cascade of thrombotic events following atherosclerotic plaque rupture causes occlusion of the coronary artery, interrupting blood supply and oxygen to myocardium thus resulting in infarction. Myocardial necrosis following infarction is followed by heart failure, myocardial rupture or arrhythmias. Early treatment of myocardial ischaemia to prevent necrosis with treatments such as fibrinolysis, coronary artery bypass grafting and percutaneous coronary intervention have improved outcome (3). Timely diagnosis allows clinicians to risk stratify their patients and select appropriate treatment. Biomarkers have been used to assist with timely diagnosis, while an increasing number of novel markers have been identified to predict outcome following an AMI or acute coronary syndrome. This may facilitate tailoring of appropriate therapy to high-risk patients (4). Various biomarkers like classically

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CPK-MB, LDH, SGOT and natriuretic peptides earlier, and recently circulating micro RNA, gene expression biomarkers, heart-type fatty acid binding protein, etc have been evaluated in AMI.

There is paucity of data available in the literature regarding another biomarker, malondialdehyde (MDA) levels in AMI patients, particularly from our country. There are conflicting reports of association of MDA levels among AMI patients: Some found decreased levels of MDA suggesting oxidative stress, while others failed to find any difference.

Aims and objectives

With this background, the present study was designed to determine whether AMI was accompanied by change in serum MDA levels.

Materials and methods:

This study was a hospital-based, case-control study conducted in the Department of Biochemistry of Murshidabad Medical College and Hospital, Berhampore, West Bengal. The study was approved by the local ethical committee and all patients and control subjects gave their informed consent to take part in this investigation.

The duration of the present study was 13 months and included 68 AMI patients. In addition, 62 healthy persons who were age- and sex-matched with the subjects served as controls. Complete history and physical examination of all cases and controls were undertaken. Exclusion criteria included smokers, kidney and liver dysfunction, obesity, patients taking antioxidants, vitamin supplements and other causes of false positive MDA.

Five milliliter of venous blood sample was collected from each case (on the third day after AMI) and control. All samples were coded and assayed in a blind fashion by an investigator who was unaware of the subjects' clinical status.

Serum MDA was assayed by TBARS method (5).

Statistical analysis of the data was performed by using Statistical Package for Social Sciences and inferences were drawn. $P < 0.05$ was considered to be significant and $p<0.001$ highly significant.

Observations and Results:

Blood was drawn from 64 patients and 59 controls because 4 patients and 3 controls dropped out from the study.

The age of patients ranged from 47 to 65 years.

No significant correlation was found between the patients' age and serum MDA levels.

There was no significant difference in MDA levels between male and female patients.

	Male	Female
Cases	3.1+0.3	3.2+0.4
Controls	2.3+0.1	2.2+0.6

Table 1. Mean MDA levels (in nmol/ml) in male and female subjects in case and control groups.

MDA levels were highly significantly greater in cases compared to controls ($p<0.001$).

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Cases	Controls
3.1+0.4	2.2+0.3

Table 2. Mean MDA levels (in nmol/ml) in case and control groups.

Discussion :

Cells continuously produce free radicals and reactive oxygen species (ROS) as part of their metabolic processes (6). ROS can be produced by either breakage of covalent bond, addition of electrons to a molecule or removal of hydrogen by other radicals. They are generally highly reactive species and typically act as electrophilic species or oxidant agents. The most important radicals or pro-oxidant molecules involved in disease processes are superoxide, hydroxyl radical, hydrogen peroxide and certain oxides of nitrogen, like nitric oxide and peroxynitrite (7). The overproduction of reactive species results in oxidative stress. In other words, it can be a combination of an increased formation of oxygen-nitrogen derived radicals and reduced antioxidant capacity, causing an imbalance that might result in the attack of cellular components, especially lipids. It has been implicated in the pathogenesis of various diseases including and atherosclerosis (8). Since it is complex measuring free radicals directly in vivo, it is necessary to carry out the quantification of cellular components which can react with these free radicals, such as lipids (9). Once lipid peroxides are unstable compounds, they tend to degrade rapidly in a variety of sub products. MDA is one of the most known secondary products of lipid peroxidation, and it can be used as a marker of cell membrane injury (10).

Kesavulu et al observed that diabetic patients with coronary heart disease had higher levels of MDA than those diabetics without this disease (11). The same research group showed that cardiovascular diseases have also been related to free radical-mediated mechanisms and to lipid peroxidation, along with the fact that they are a major cause of mortality and morbidity in hemodialysis patients. In another study, patients with lesser degree of heart failure showed significantly lower MDA levels and significantly higher levels of vitamin A, vitamin E, lutein, and lycopene than patients with higher degree of heart failure (12). van den Berg et al found that serum levels of IgG and IgM autoantibodies against malondialdehyde low density lipoprotein were associated with clinical coronary heart disease and unfavorable plaque characteristics (13). Some researchers proposed that plasma levels of MDA-modified LDL were significantly higher in patients with acute coronary syndromes than in individuals with stable coronary artery disease (14). The present study found greater levels of MDA in AMI cases compared to healthy controls and the difference was statistically highly significant (Table 2), though there was no statistically significant difference in MDA levels between male and female subjects in both case and control groups (Table 1). This finding might indicate more production of lipid peroxidation products in AMI. The "in vivo" relevance of the increased serum MDA in the post-infarct period is unknown at the present, but as lipid peroxides are known to harm cellular structures and to inhibit prostacyclin synthesis, it may be of interest with regard to the long term secondary effects in AMI patients. As free radical-induced damage is thought to be one of the important factors in the etiopathogenesis of LP, in our opinion, treatment guidelines should include optimal strengthening of antioxidant defense. Anderson

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et al concluded that IgM, IgG and IgA anti- Malondialdehyde-acetaldehyde adducts -HSA antibody isotypes are differentially and significantly associated with AMI and may serve as biomarkers of atherosclerotic disease (15). Amir et al identified specific peptides that are immunological mimotopes of MDA, which can serve as standardized and reproducible antigens that will be useful for diagnostic and therapeutic applications in cardiovascular disease (16).

This study has limitations that must be considered. To assess MDA, TBARS method was used. MDA can be estimated by various methods, but the present method was employed as it is the most commonly used, time tested and standard method. Also, number of patients in the study groups was not large. Thus, care must be taken in extrapolating the present findings to other populations. Despite these limitations, we believe that our study points towards using it as an important, promising free radical marker for AMI. As our findings point to a increase in the free radical MDA, the problem of oxidative stress in AMI should also be further investigated in a larger number of patients, and other markers of oxidative stress and antioxidants should be assessed.

Conclusions:

The results of our study suggest that AMI may be related to raise of MDA levels in serum. MDA may be considered as a useful biomarker of free radical status in AMI for elaboration of treatment strategy and monitoring.

References:

1. White HD, Chew DP. Acute myocardial infarction. Lancet. 2008 Aug 16;372(9638):570-84.

2. Deedwania P, Singh V. Coronary heart disease in South Asians: evolving strategies for treatment and prevention. Indian Heart J 2005;57:617–631.

3. Tunstall-Pedoe H, Vanuzzo D, Hobbs M, Mahonen M, Cepaitis Z, Kuulasmaa K, Keil U: Estimation of contribution of changes in coronary care to improving survival, event rates, and coronary heart disease mortality across the WHO MONICA Project populations. Lancet. 2000, 355: 688-700

4. Chan, D., Ng, L.L. Biomarkers in acute myocardial infarction. BMC Med 8, 34 (2010).

5. Placer ZA, Cushman LL, Johnson BC. Estimation of product of lipid peroxidation (malonyl dialdehyde) in biochemical systems. Anal Biochem. 1966 Aug;16(2):359-64

6. Urso, M .L.; Clarkson, P. M.; Toxicology 2003, 189, 41

7. Gillham, B.; Papachristodoulou, D. K.; Thomas, J. H.; Will's: Biochemical basis of medicine, 3rd ed., Butterworth-Heinemann: Oxford, 1997.

8. Halliwell, B.; Br. Med. J. 1993, 307, 885.

9. Esterbauer, H.; Cheeseman, K. H.; Methods Enzymol. 1990, 186, 407.

10. Esterbauer, H.; Schaur, R. J.; Zollner, H.; Free Radical Biol. Med. 1991, 11, 81.

11. Kesavulu, M. M.; Rao, B. K.; Giri, R.; Vijaya, J.; Subramanyam, G.; Apparao, C.; Diabetes Res. Clin. Pract. 2001, 53, 33

12. Polidori MC, Savino K, Alunni G, Freddio M, Senin U, Sies H, Stahl W, Mecocci P. Plasma lipophilic antioxidants and malondialdehyde in congestive heart failure patients: relationship to disease severity. Free Radic Biol Med. 2002 Jan 15;32(2):148-52.

13. van den Berg VJ, Haskard DO, Fedorowski A, Hartley A, Kardys I, Caga-Anan M, et al. IgM anti-malondialdehyde low density lipoprotein antibody levels indicate coronary heart disease and necrotic core characteristics in the Nordic Diltiazem (NORDIL) study and the Integrated Imaging and Biomarker Study 3 (IBIS-3). EBioMedicine. 2018 Oct;36:63-72

14. Holvoet P, Vanhaecke J, Janssens S, Van de Werf F, Collen D. Oxidized LDL and malondialdehyde-modified LDL in patients with acute coronary syndromes and stable coronary artery disease. Circulation. 1998 Oct 13;98(15):1487-94

15. Anderson DR, Duryee MJ, Shurmur SW, et al. Unique antibody responses to malondialdehyde-acetaldehyde (MAA)-protein adducts predict coronary artery disease. PLoS One. 2014;9(9):e107440. Published 2014 Sep 11. doi:10.1371/journal.pone.0107440

16. Amir S, Hartvigsen K, Gonen A, Leibundgut G, Que X, Jensen-Jarolim E, Wagner O, Tsimikas S, Witztum JL, Binder CJ. Peptide mimotopes of malondialdehyde epitopes for clinical applications in cardiovascular disease. J Lipid Res. 2012 Jul;53(7):1316-26.