Study of levels of malondialdehyde (MDA) among pateints with acute myocardial infarction

Dr.Wajdy J Majid , Dep.of biochemistry,Thiqar college of medicine

SUMMARY : Serum malondialdehyde (MDA), as an index of lipid peroxidation, and the serum enzymes creatinin kinase (CK) , lactate dehydrogenase (LDH), were evaluated in a group of 32 patients with acute myocardial infarction (AMI) , 12 with angina pectoris (AP), and 88 healthy subjects as a control group . MDA values were within the normal range in those with angina pectoris patients, while in those with acute myocardial infarction patients a significant increase in serum MDA was observed in the days following the acute event, reaching a peak level in 6-8 days later, a significant relation was found between the integrated concentration-time MDA curve and the integrated serum enzymes activity curves reached during the nine days after the acute event. 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.

Introduction

Malondialdehyde is a known stable product of lipidperoxidation. (1,2) Therefore,the evaluation of the malondiadehyde by the thiobarbituric acid reaction may be used to decide wherther a process of lipid peroxidation has taken place.lipid peroxidation is thought to be involved in various pathological conditions, among other, platelet activation,(3) tissue destruction (4) and various Inflammatory processes.(5)

Since acute myocardial infarction (AMI) may be related to a thromboembolic process,(6) to tissular destruction, and to asecondary inflammatory process, it seemed of the patients. In order to evaluate this possibility, serum MDA was quantified in a group of AMI.

Free radicals are atoms or moleccules that contains one or more unpaired electrons (3).

The presence of unpaired electrons make the species highly reactive(3). They play an important role in human diseases(4). Free radicals include free oxygen related reaction compounds collectively known as "Reactive Oxygen Species" (ROS)(3). The reactive oxygen includes superoxide, hydrogen peroxide (HO), hydroxyl(OH) and the superoxide radicals which is formed when electrons leak from the electron transport chain(4).The dismutation of superoxide(O) results in the formation of 2 hydrogen peroxide. The hydroxyl ion is highly reactive and can modify purines and pyrimidines that cause strand breaks resulting in DNA damage(5). Some oxidase enzymes can directly generate the hydrogen peroxide radical(4).Free radicals resul in peroxidation of polyunsaturated fatty acids in the cell membrane and subsequent generation of further unstable radicals leading to a chain of events. This attack makes cell membrane leaky and the functions of absorption and secretion are lost that finaly leads to cell death [4].In those patients with acute myocardial infarction, the balance between pro oxidant and anti oxidant capacity is shifted towards an increased oxidative stress(6).

Matrial and methods:

MDA values were studied in apopulation of 88 normal fasting subjects between the ages of 23 and 70 (40 men with mean age=45 year,and 48 women with mean age=42 year) in AL-Hussein teaching hospital, all without cardiovascular or haematological complications and without diabetes, dyslipidemias or other metabolic disorders. All control subjects those are studied having receivind any medication known to modify platelet function in the 15 days prior to sampling.

PATIENTS:

Fourty - four (44) patients were studied between April 2011 and January 2012 , they were classified into two groups : 32 patients with AMI (17 men with mean age = 55 year and 15 women with mean age = 60 year) , and 12 patients with angina pectoris (AP) (7 men with mean age = 49 year and 5 women with mean age = 65 year) , diagnosed according to usual electrocardiographic, enzymatic and clinical criteria.(7) Samples were taken from the cubital vein of each patient on various days from the time of their admission up to nine days afterwards in the case of AMI patients, and up to four days after admission in the case of AP patients. In order to study the daily evolution of the patients and to locate the correct timing

of the determinations, the zero reference point was taken to be the moment the precordial pain appeared, according to the patient's statement.

The MDA was evaluated by using the thiobarbituric acid based procedure described by Wasowicz et al (8) , 50 µl of plasma are added to 0.95 bidistilled water followed by addition of 1 ml of solution containing 29 mmol thiobarbituric acid in 8.75 mol/l acetic Acid. Sample are heated for 60 minuts at 95 c and cooled down, then 25 µl of solution containing 5 mol/l hydrochloric acid is added. After adding of 3 ml 1-butanol, sample are centrifuged (1000xg, 10 min) and fluorescence measured (wxcitation wave length : 525 nm, emission wave length 547 nm).(8)Concentrations of serum creatinine kinase (CK) estimated by enzymatic method described by Oliver and modified by Rosalki and later by Szasz , the increase in in absorbance , proportional to CK activity in the specimen , is measured at 340 nm . (9,10 ,11) lactate dehydrogenase (LDH) catalyses the reduction of pyruvate by NADH according to the following reaction :

Pyruvate + NADH + H+ → L-lactate + NAD+ The rate of decrease in concentration of NADPH measured photometric ally, is proportional to the catalytic concentration of LDH present in the sampl e .(12,13,14) . Plasma values of MDA from normal subjects were arranged in a percentile cumulativ frequency Linear correlation and Simson's curve integration method

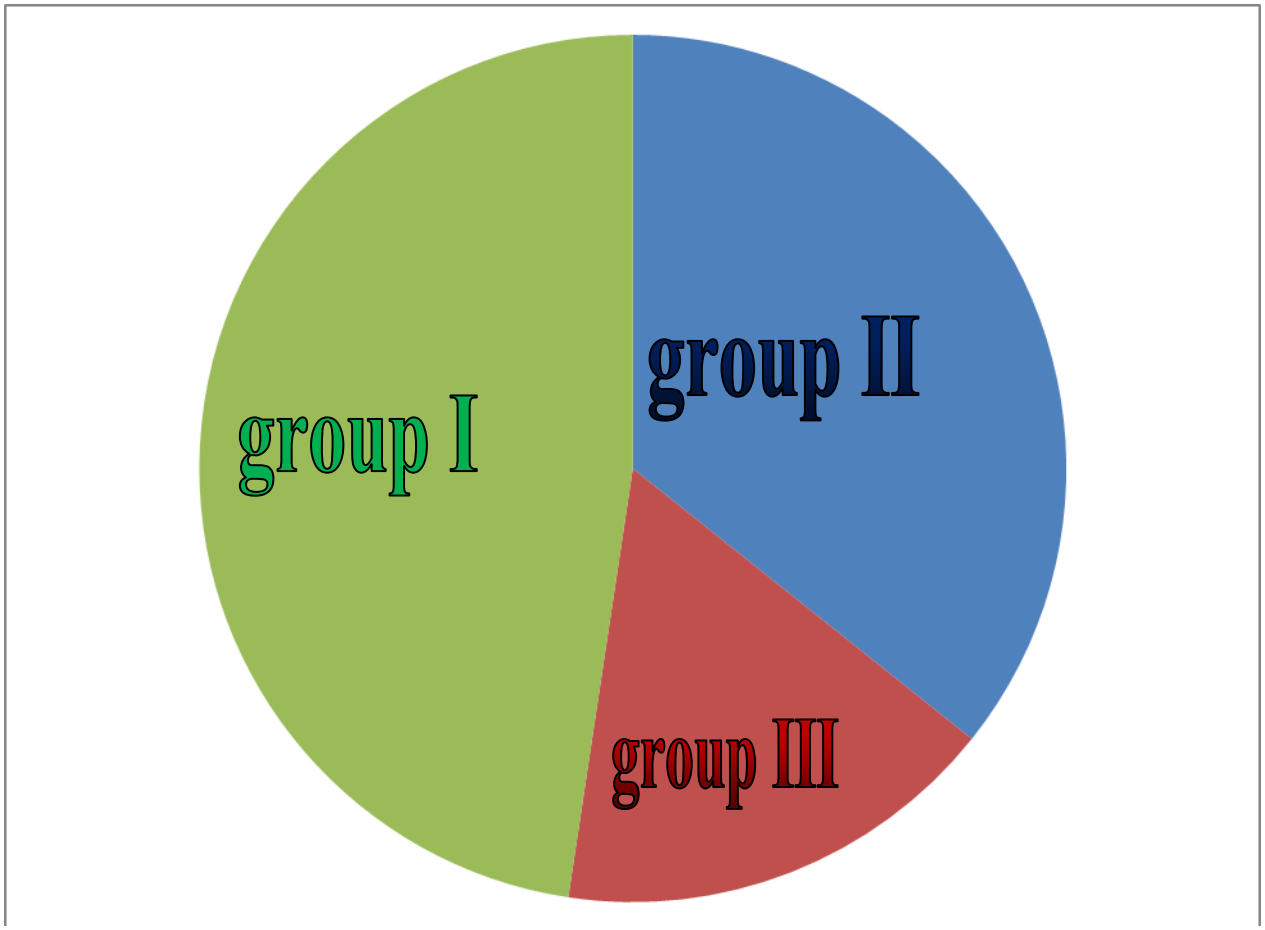
Were used for statistical analysis

Results

All the participants in this study were classified into three groups as shown in (Fig.I) , while the characteristics of the study shown in (Table I) . The mean value of serum MDA in the control group was mean = 32- 56 . The mean serum MDA concentrations in the AMI and AP patients within the first 24 hour of the onset of the precordial pain were within the normal control range in both groups (Fig. II), while on the days after the acute event an increase in the serum MDA was observed in the AMI patients, reaching its maximum on the eighth day (Fig.II). The values of patients with AP don't vary significantly and were within the normal control range on the days the determinations were performed (Fig.II). The percentage of patients having MDA concentrationshigher than 61 nmol /ml, taken as the upper normal limit in this laboratory (upper normal limit = mean 2SD) increases to a maximum of 90% on the seventh and eighth days. The percentage of AP patients with serum MDA concentrations higher than 61 nmol / ml after the acute crisis, was much lower than that of the AMI patients, with no apparent increase over the days after the acute event as in the AMI patients . With the object of evaluating the possible relation between the serum MDA concentrations observed in the AMI patients with the cardiac lesion, the enzyme activities-time curves of CPK,

LDH, and the concentration-time MDA curve were studied in 22 of the AMI patients from the acute event up to the ninth day after (Fig.II) .concentration- time MDA curve and the integrated activities-time curves of CPK, LDH, astatistically significant correlation (0-01>p > 0-001) was also found between the integrated curves.

(Figure I): three groups of all participants for the study



group I : 88 normal subjects as a control group
group II : 32 patients with AMI
group III : 12 patients with AP

Table I: charecterstic of the study

Variable	group I	group II	group III
Age	23 – 70 year	55 – 60 year	49 – 65 year
Sex	40 men 48 woman	17 men 15 woman	7 men 5 woman
MDA	33 – 58 nmol /ml	54 – 88 nmol / ml	23 – 69 nmol / ml
C P K	42 – 145 U / L	98 – 295 U / L	48 – 171 U /L
L D H	238 - 472 U/ L	343 – 992 U / L	244 – 481 U / L

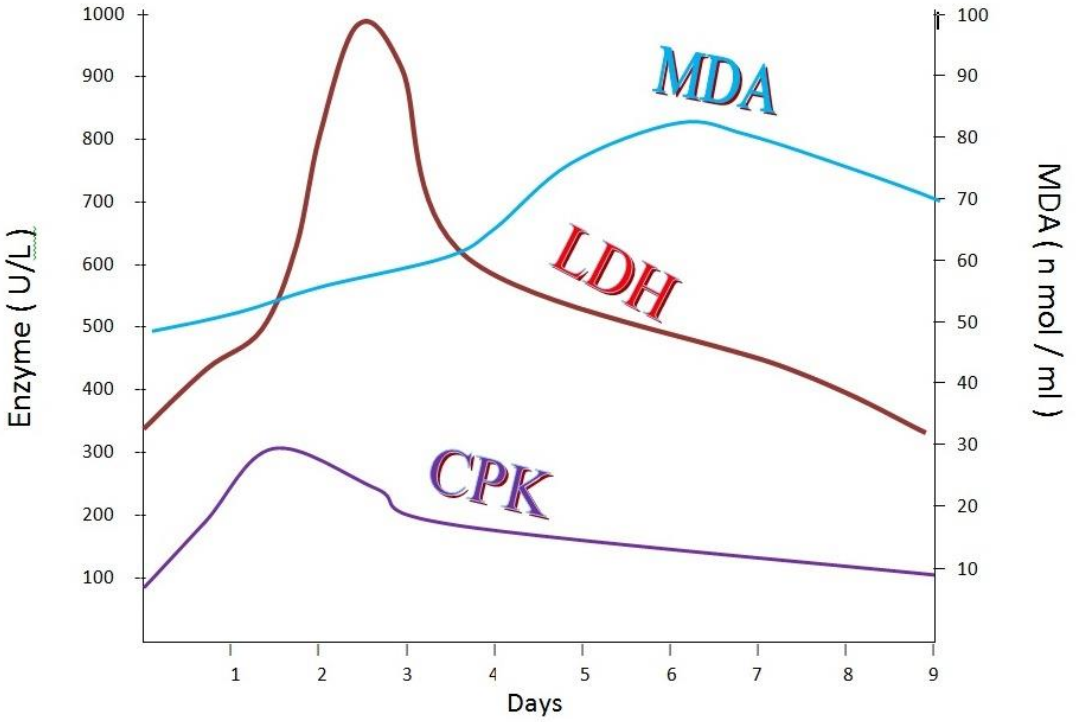


Figure II : MDA conc. Time curve and enzymes activity time-curve of CPK , LDH on the nine day following the acute event .

DISCUSSION

The results show that within the first 24 hours of chest pain ,the serum concentration of MDA in the AMI group and AP group are within normal range, and then gradually increasing in its value in AMI group with maximum level at 7^{th} to 8^{th} Days.

If one considers that the activities of the serum enzymes related to cardiac damage have a relation with the size of the lesion,('15) the correlation found between the integrated area of the MDA concentration-time curve and cardiac enzymes activity-time curves could suggest a certain relation between MDA and cardiac damage.

The origin of this increase in MDA is unknown, although it may be related to an increase in prostaglandin synthesis (16) since processes such as myocardial ischaemia ,(17),hypoxia,(18), inflammatory processes'(19) and platelet aggregation,(3) circumstances which may occur in AMI patients have been reported to cause an increase in prostaglandin release, however other mechanisms of lipid peroxidation cannot be excluded. It has been shown that lipid peroxides(20) and the stable breakdown product of lipid peroxidation MDA (21,22)' could be transported by low density lipo proteins (LDL), and also that the MDA bound to LDL favour the incorporation of cholesterol esters in the cells of the atherosclerotic reaction(.22)

Additionally, lipid peroxides are known to harm cellular and tissular components (23 24) and to inhibit prostacyclin biosynthesis.(25) Therefore, the observed increase in serum MDA in AMI patients may be an additional risk factor in those subjects as the possible incorporation of lipid peroxides into the arterial wall could reduce the vascular antiaggregant defence and could favor the development of the aherosclerotic lesion. Although further investigations are needed to assess the biological and long term significance of the observed increase in MDA in AMI patients, the inclusion of an antioxidant might be reasonably considered in the therapeutic treatment of those patients.(25)

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دراسة مستويات المالونداي الديهايد عند مرضى احتشاء عضلة القلب الحاد في مدينة الناصرية

د.وجدي جبار ماجد , فرع الكيمياء السريريه , كلية طب ذي قار

الموجز:

مصل المالونداي الديهايد كمؤشر لبيروكسيد الدهون، كذلك الانزيمات في الدم الكرياتينين كيناز و نازعة اكتات جرى تقييمهم في مجموعة من 32 مريضا باحتشاء عضلة القلب الحاد و 12 مريضا بالذبحة الصدرية ، و 88 شخصا سليما كمجموعه ضابطه . كانت قيم المالونداي الديهايد ضمن المعدل الطبيعي في مرضى الذبحة الصدرية ، بينما في مرضى احتشاء عضلة القلب الحاد لوحظ زيادة كبيرة في المصل المالونداي الديهايد في الأيام التي تلت هذا الحدث الحاد، وبلغ الحد الأقصى 6-8 أيام في وقت لاحق، وجدت علاقة احصائيه معتبره ين المالونداي الديهايد المتكامل مع منحني فعالية انزيمات مصل الدم المتكامل التي تم قياسها خلال منحنى تركيز زيادة مصل المالونداي الديهايد في التسعة ايام التاليه لحدوث النوبه الحاده . و"في الجسم الحي" أهمية فترة ما بعد الاحتشاء غير معروف في الوقت الحاضر، ولكن كما هي معروفة البيروكسيدات الدهنية لإلحاق الضرر بتركيب الهياكل الخلوية و لمنع صنع بروستاسيكلين.