

Serum malondialdehyde-like material (MDA-LM) in acute myocardial infarction

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SUMMARY Serum malondialdehyde-like material (MDA-LM), as an index of lipid peroxidation, and the serum enzymes CK, CK-MB, LDH, LDH₁ and, α -HBDH were evaluated in a group of 26 patients with acute myocardial infarction (AMI), seven with angina pectoris (AP), and in a normal control group of 94 subjects. MDA-LM values were within the normal range in AP patients, while in AMI patients a significant increase in serum MDA-LM was observed in the days following the acute event, reaching a maximum 6-8 days later, when 90% of the patients had values higher than the upper normal limit (mean \pm 2SD) of the control group.

A significant correlation was found between the integrated concentration-time MDA-LM 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-LM 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.

Malondialdehyde is a known stable product of lipid peroxidation.^{1,2} Therefore, the evaluation of the malondialdehyde-like material (MDA-LM) by the thiobarbituric acid reaction may be used to decide whether a process of lipid peroxidation has taken place.

Lipid peroxidation is thought to be involved in various pathological conditions, among others, platelet activation,³ tissue destruction⁴ and various inflammatory processes.⁵

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

Material and methods

MDA-LM values were studied in a population of 94 normal fasting subjects between the ages of 23 and 70 (40 men, mean = 45 yr, and 54 women, mean =

42 yr), from the Preventive Medicine Clinic in our Hospital, all without cardiovascular or haematological complications and without diabetes, dislipaemias or other metabolic disorders. All control subjects studied denied having received any medication known to modify platelet function in the 15 days prior to sampling.

PATIENTS

Thirty-three patients were studied. They were classified into two groups: 26 patients with AMI (17 men, mean = 55 yr; 9 women, mean = 60 yr), and seven patients with angina pectoris (AP) (4 men, mean = 49 yr; 3 women, mean = 65 yr), diagnosed according to usual electrocardiographic, enzymatic and clinical criteria.⁷ The only criterion for admission of the patients into the study was the diagnosis of AMI or AP during the time the project was being carried out.

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

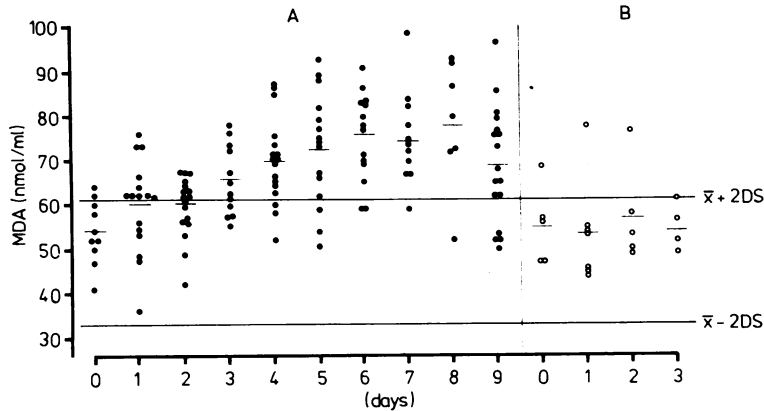


Fig. 1 MDA-LM values (nmol/ml) on the days following the acute event in a group of patients with acute myocardial infarction (A) and angina pectoris (B). Zero (0) corresponds to determinations performed less than 24 h after the onset of the precordial pain. Mean \pm 2SD is the discrimination limit of the MDA-LM level found in the 94 control subjects studied (47.18 ± 6.96 nmol/ml)

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-LM was evaluated by the thiobarbituric acid reaction according to the method previously described.⁸

Concentrations of serum creatinine kinase (EC 2.7.3.2) (CK),⁹ lactate dehydrogenase (EC 1.1.1.27) (LDH)¹⁰ and α -hydroxybutyric dehydrogenase (EC 1.1.1.30) (α -HBDH)¹¹ were evaluated in an LKB 8.200 Autoanalyzer.

Serum CK and LDH isoenzymatic activities were determined as described previously by Elevitch¹²⁻¹⁴

Plasma values of MDA-LM from normal subjects were arranged in a percentile cumulative frequency. Linear correlation and Simson's curve integration method were used for statistical analysis.

Results

The mean value of serum MDA-LM in the control group was mean = 47.18 , SD = 6.96 nmol/ml. The mean serum MDA-LM concentrations in the AMI and AP patients within 24 h of the onset of the precordial pain were within the normal control range in both groups (Fig. 1), while on the days after the acute event an increase in the serum MDA-LM was observed in the AMI patients, reaching its maximum on the eighth day (Fig. 1). The values of the AP patients did not vary significantly and were within the normal control range on the days the determinations were performed (Fig. 1).

The percentage of patients having MDA-LM concentrations higher than 61 nmol/ml, taken as the upper normal limit in this laboratory (upper normal limit = mean \pm 2SD) increases to a maximum of 90% on the seventh and eighth days. The percentage of AP patients with serum MDA-LM 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 (Fig. 1).

With the object of evaluating the possible relation between the serum MDA-LM concentrations observed in the AMI patients with the cardiac lesion, the enzyme activities-time curves of CPK, LDH, and α -HBDH and the concentration-time MDA-LM curve were studied in 21 of the AMI patients from the acute event up to the ninth day after (Fig. 2). The MDA-LM concentration and the enzyme activities show a distinct pattern of evolution during the days after the acute event. However, when we studied the possible linear correlation between the integrated areas of the enzyme activities-time curves and the integrated concentration-time MDA-LM curve (Table), a statistically significant correlation was found between the integrated concentration-time MDA-LM curve and the integrated activities-time curves of CPK, LDH, α -HBDH, as well as that of the isoenzyme LDH₁. A statistically significant correlation ($r = 0.562$, $0.01 > p > 0.001$) was also found between the integrated curves of serum MDA-LM concentration and CK-MB activity obtained in the days when the CK-MB activity was other than zero.

Table Integrated areas under the MDA-LM concentration-time and enzymes activity-time curves of each of the AMI patients studied

MDA	CPK	LDH	LDH ₁ †	α-HBDH
921.84	462.5	3789	425	1905
534.91	882.5	11551.5	364	223
679.80	1555.5	9854	585.5	6772
112.46	178	590	54.5	290
583.14	736	5671	330	4021.5
405.99	306.2	4415.5	305.5	2942
552.36	681.6	4787.5	366.5	2676.5
640.6	1207	5424.5	347	2930
518.54	434	3556.5	365	2166
1388.72	1777.8	9245.5	461.5	6426
487.91	346.5	3026	330	3554.5
116.76	242	1582	66.5	891.5
338.07	591.5	3201	182.5	2018
807.95	174.5	4090	323	2276
573.07	510	4440	241.5	2654.5
496.55	1179.5	5047	301.5	2520.5
146.07	455.5	4405	76.5	1103
594.44	575	3648	272	2266
793.07	912	8141	473.5	5292
347.08	466.5	2283.5	167.5	1250

MDA/CPK	r = 0.612*			
MDA/LDH		r = 0.575*		
MDA/LDH ₁			r = 0.785**	
MDA/HBDH				r = 0.676**

r = linear correlation coefficient between MDA-LM concentration-time and enzyme activity-time curves integrated areas.

*0.01 > p > 0.001

**p < 0.001

†Activity referred to percentage of total LDH.

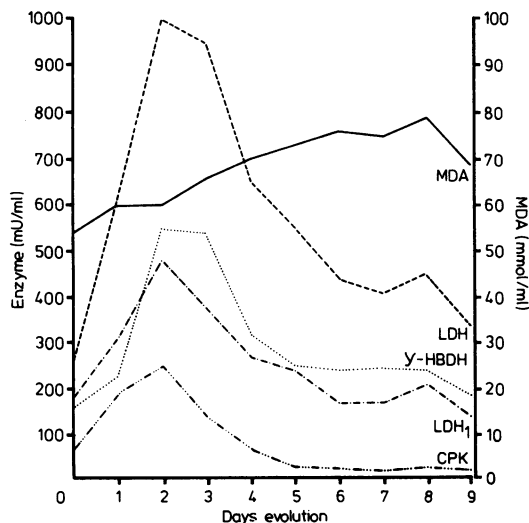


Fig. 2 MDA-LM concentration (nmol/ml)-time curve and enzyme activity (mU/l)-time curves of CK, CK-MB, LDH, LDH₁ and α-HBDH on the nine days following the acute event.

Discussion

The results show that within 24 hours of the appearance of the precordial pain the serum MDA-LM

concentrations in the AMI and AP patients, although slightly higher, are within the range of the normal control group. The fact that the MDA-LM concentrations progressively increase during the days following the acute event, reaching maximum values in 6–8 days, suggests that the increase is secondary to the acute crisis; this MDA-LM increase could be related to the myocardial lesion or in general to the alterations which are secondary to AMI.

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-LM concentration-time curve and cardiac enzymes activity-time curves could suggest a certain relation between MDA-LM and cardiac damage.

The origin of this increase in MDA-LM is unknown, although it may be related to an increase in prostaglandin synthesis,¹⁶ since processes such as myocardial ischaemia,¹⁷ hypoxia,¹⁸ inflammatory processes¹⁹ 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 peroxides²⁰ and the stable breakdown product of lipid peroxidation MDA^{21 22} could be transported by low density lipoproteins (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-LM 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 favour the development of the atherosclerotic lesion. Although further investigations are needed to assess the biological and long term significance of the observed increase in MDA-LM in AMI patients, the inclusion of an antioxidant might be reasonably considered in the therapeutic treatment of those patients.

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