

Plasma free fatty acid and catecholamine levels in patients with acute myocardial infarction

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In 25 men with acute myocardial infarction simultaneous determinations of free fatty acid (FFA), noradrenaline, and adrenaline were made in blood samples obtained on the 1st and the 10th day after the acute attack. In the acute phase of myocardial infarction the levels of FFA and noradrenaline were significantly higher than on the 10th day of illness and revealed a highly significant positive correlation. The blood adrenaline levels were not significantly raised and did not correlate with the FFA levels. Probable mechanisms and significance of metabolic changes occurring in the acute phase of myocardial infarction are discussed.

Acute myocardial infarction is accompanied by profound metabolic changes. It is now well established that the activity of the sympatho-adrenal system is increased in acute myocardial infarction, as reflected in augmented urinary excretion of noradrenaline and adrenaline and raised plasma levels of these catecholamines (Januszewicz *et al.*, 1968; Klein *et al.*, 1968; McDonald *et al.*, 1969; Valori, Thomas, and Shillingford, 1967a, b). It was also shown that the excretion of catecholamines might vary in relation to the severity of the clinical course and to the nature of concomitant complications (Januszewicz *et al.*, 1968; Jewitt *et al.*, 1969; Valori *et al.*, 1967a, b). Recently, attention has been paid to the increased plasma free fatty acids (FFA) in patients with acute myocardial infarction (Gupta *et al.*, 1969; Kurien and Oliver, 1966; Oliver, Kurien, and Greenwood, 1968). The observations on the higher incidence of cardiac arrhythmias and sudden death in patients with myocardial infarction exhibiting strikingly raised serum FFA are particularly noteworthy (Gupta *et al.*, 1969; Oliver *et al.*, 1968; Oliver, 1968). Other authors have not found a relation between the initial rise of plasma FFA and the subsequent clinical course of acute myocardial infarction; however, they have noted a repeated increase of plasma FFA coinciding with the onset of complications (Rutenberg, Pamintuan, and Soloff, 1969). It seems probable that the increase of plasma FFA under

these circumstances is related to augmented secretion of catecholamines. The present study was undertaken to investigate a possible relation between the increase of plasma FFA and that of plasma catecholamines in acute myocardial infarction.

Patients and methods

Twenty-five men with acute myocardial infarction, consecutively admitted to the coronary care unit, were studied. The age range was 35-65 years, with a mean of 51.4 years. The diagnosis of myocardial infarction was based on the clinical picture, typical electrocardiographic findings, and raised enzyme levels. None of the patients received heparin, corticosteroids, clofibrate, glucose infusions, or other drugs which might have influenced the parameters studied. None of the patients had a history of diabetes mellitus. The patients were continuously monitored with an oscilloscope, with frequent pulse and blood pressure measurements. The venous blood samples of about 25 ml were obtained within 12 hours from the onset of the acute attack, at least 5 hours after a meal. The infarction was transmural in 22 patients and subendocardial in 3 patients. The localization of the infarction was anterior in 8 patients, anterolateral and inferolateral in 2 patients each, and inferior in 8 patients. None of the patients had evidence of shock. Four patients gave a history of hypertension. In 4 patients the systolic blood pressure was 160 mmHg or higher, and in 10 patients the diastolic blood pressure equalled or exceeded 95 mmHg at the time of blood collection.

Various degrees of heart failure were found in 18 patients; in 12 of them the symptoms of heart

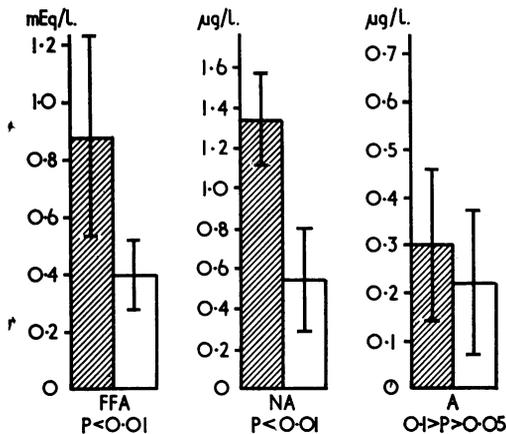


FIG. Mean values of free fatty acids (FFA), noradrenaline (NA), and adrenaline (A). Shaded blocks represent the 1st day and open blocks the 10th day of observation. Vertical lines represent standard deviation.

Euler and Lishajko (1961). The normal plasma concentrations of noradrenaline and adrenaline according to this laboratory are $0.67 \pm 0.3 \mu\text{g/l}$. and $0.22 \pm 0.09 \mu\text{g/l}$., respectively. Plasma FFA concentration was determined by the method of Dole (1956). The results were subjected to statistical analysis; the differences were considered statistically significant when the P index was less than 0.05. Mean values are followed by \pm which mean standard deviation.

Results

The plasma FFA levels in the first 24 hours of acute myocardial infarction ranged from 0.225 to 2.303 mEq/l., with the mean of 0.874 ± 0.343 mEq/l. The simultaneously measured plasma levels of noradrenaline ranged from 0.52 to 2.80 µg/l., with the mean of 1.34 ± 0.22 µg/l. and those of adrenaline ranged from 0.12 to 0.95 µg/l., with the mean of 0.30 ± 0.16 µg/l.

The corresponding control values, found 10 days after the onset of infarction, were: FFA: 0.208–0.726, mean 0.387 ± 0.122 mEq/l.; noradrenaline: 0.20–0.99, mean 0.53 ± 0.26 µg/l.; adrenaline: 0.10–0.90, mean 0.22 ± 0.15 µg/l.

The statistical analysis revealed that the differences between the first and the tenth day of myocardial infarction were significant for noradrenaline ($P < 0.01$), and FFA ($P < 0.01$); the difference in plasma adrenaline was not statistically significant ($P > 0.05$) (Fig.). A highly significant positive correlation was found between the plasma concentrations of FFA and noradrenaline in the early acute stage of myocardial infarction ($r = +0.741$; $P < 0.01$). The plasma FFA and adrenaline did not correlate ($r = +0.010$; $P > 0.1$).

Discussion

In accordance with the reports of other authors (Gupta *et al.*, 1969; Kurien and Oliver, 1966; Oliver, 1968; Rutenberg *et al.*, 1969), our study showed a significant increase in plasma FFA in the first 24 hours of acute myocardial infarction with subsequent normalization on the 10th day. The difference between the first and the tenth day was statistically highly significant. Similarly, the plasma noradrenaline concentration was significantly raised on the 1st day in comparison with the 10th day. The highly significant correlation between the concentrations of noradrenaline and FFA, found in the acute stage of myocardial infarction, and the parallel decline of these values in time deserve particular attention. On the other hand, the plasma adrenaline concentration increased slightly and did not correlate with plasma FFA.

failure subsided within a few days. One patient was admitted with intractable pulmonary oedema. Cardiac arrhythmias were found in 13 patients; in 4 patients they were multiple. There were 2 cases of atrial fibrillation and 1 case of ventricular fibrillation successfully treated by direct current countershock. Four patients had ventricular ectopic beats of a frequency exceeding 1:10. Three patients were found to have 1st or 2nd degree atrioventricular block which, in 2 of them, increased periodically to complete atrioventricular block. Out of the 25 patients studied, 4 died. In 1 case death was due to cardiac rupture within the first 24 hours, in 2 cases to intractable pulmonary oedema; one patient died with symptoms of septicaemia. In 23 patients control blood samples were obtained 10 days after the onset of acute myocardial infarction. At the time of the control blood collection, none of the patients experienced angina; heart failure persisted in 2 patients and arrhythmia was still present in 2 patients who had infrequent ventricular and supraventricular ectopic beats.

Plasma noradrenaline (recovery $85 \pm 2.9\%$) and adrenaline (recovery $81 \pm 1.7\%$) were determined fluorometrically by the method of Vendsalu (1960). 18 ml blood were collected into a siliconized test-tube containing 2 ml 1 per cent EDTA with the addition of a small amount of metabisulphite sodium. After the blood had been deproteinized by the addition of 0.4 N perchloric acid, it was centrifuged for 10 minutes at 10° C. The catecholamines were then isolated from the sample by means of column chromatography on Dowex-X4 200 mesh. After the column had been activated, the catecholamines were eluted with 1 N hydrochloric acid. The quantitative estimation of noradrenaline and adrenaline in the eluate was performed with the trihydroxyl method of

The mechanism and the significance of the increase of plasma FFA concentration in acute myocardial infarction has been a matter of interest, especially so in connexion with the role of FFA in the myocardial metabolism. The increased circulating plasma FFA promote augmented myocardial oxygen consumption which may be particularly harmful for ischaemic myocardium. A relation between the post-heparin increase of plasma FFA and the incidence of cardiac arrhythmias was reported in dogs with acute coronary artery occlusion (Kurien, Yates, and Oliver, 1969). It was also shown that in experimental conditions the FFA diminish the contractility of the hypoxic heart muscle (Henderson, Most, and Sonnenblick, 1969). Several recent clinical observations suggest that free fatty acids may also play an important role in the clinical course of acute myocardial infarction. In the present study we were particularly concerned with the relation between plasma FFA and catecholamine concentrations in acute myocardial infarction. In a previous report (Januszewicz *et al.*, 1968) we were able to show an augmented urinary excretion of catecholamines in acute myocardial infarction and the relation between the excretion of respective catecholamines and the severity of the clinical course and the nature of complications. Estimation of plasma catecholamine concentrations is technically more complicated than that of urinary excretion, and it does not reflect diurnal variations of the sympatho-adrenal system. However, better insight into the existing interrelations and directions of changes can be gained when several parameters are measured in the same blood sample.

It is known that noradrenaline is one of the most potent factors releasing FFA into the blood through the activation of tissue lipase and the subsequent hydrolysis of triglycerides. The highly significant correlation between the increased levels of FFA and noradrenaline which we have been able to show in the acute stage of myocardial infarction, as well as the subsequent parallel decrease of these levels, justifies the suggestion that the raised plasma FFA in acute myocardial infarction may be related to the increased noradrenaline production caused by the augmented activity of the sympatho-adrenal system in response to the infarction.

The assessment of the relation between plasma FFA and catecholamine concentration and the clinical course of acute myocardial infarction is beyond the scope of this investi-

gation. Further studies are in progress to get information on ultimate prognosis in acute myocardial infarction in relation to the magnitude of metabolic changes in the acute phase of the disease.

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