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Effect of early oral feeding on plasma free fatty acid concentrations in patients in a coronary care unit

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Forty-two consecutive patients with acute myocardial infarction were studied over the first 3 days of their illness to determine the effect of oral or intravenous calorie intake on the circulating free fatty acid values. Repeated sampling in 9 patients showed that free fatty acid levels above 1000 μmol/l were seldom found beyond the first 10 hours after admission. Oral calories, chiefly in the form of carbohydrate, reduced free fatty acid by an average of 145 μmol/l for each intake of 90 or more calories (378 kJ) on the first day. Oral calories (especially carbohydrate) should be considered as possible antilipolytic therapy if it be held desirable to reduce circulating free fatty acid concentrations in patients with acute myocardial infarction.

Should a patient in the early stages of acute myocardial infarction be fed by mouth or not? Standard advice has been semi-starvation for the first few days, followed by an 800-kcal (3.4 MJ) diet (Master, Jaffe, and Dack, 1936). Paul Wood (1952) allowed only fruit drinks and soft, stewed, or fresh fruit with sugar for the first 48 hours. Though rapid advances have been made in the application of modern technological advances to patients in coronary care units, the question of diet is usually not discussed. Starvation leads to raised plasma free fatty acid values, and we have previously shown (Gupta *et al.*, 1969) a relation between free fatty acid concentrations above 1000 μmol/l and the tendency to develop arrhythmias in patients in a coronary care unit. Our findings supported the earlier contention of Oliver, Kurien, and Greenwood (1968) that free fatty acid values above 1200 μmol/l were associated with increased arrhythmias, though there have been several other studies failing to show such an association. Kurien and Oliver (1970) ascribed a direct arrhythmogenic role to free fatty acid, but we reserved judgment and pointed out that sicker patients with greater secretion rates of catecholamines were also likely to have higher free fatty acid values. In addition, sicker patients would tend to eat less and thereby be more starved, again with higher free fatty acid values. Both blood catecholamine and insulin concentrations must be known to predict the free fatty acid value (Christensen and Videbaek, 1974). The role of circulating free fatty acids in precipitating complications of acute myocardial infarction remains very controversial (Opie and Lubbe, 1975), but the balance of present evidence is held to favour the possibility of free fatty acid 'toxicity' (Opie, 1975).

We have, therefore, examined the relation between oral intake of calories and plasma free fatty acid concentrations in patients with acute myocardial infarction. To assess the effect of feeding on plasma free fatty acids, we repeatedly sampled venous blood to obtain the circulating plasma free fatty acid values over 60 hours in patients in a coronary care unit, with special attention to the possibility that random peaks of free fatty acid values might be missed if only morning fasting samples were taken. We also measured the free fatty acid: albumin molar ratios in such patients, because of recent suggestions (Willebrands, Ter Welle, and Tasseron, 1973) that it is not only the absolute concentration of free fatty acids reaching the heart that is important but also the free fatty acid: albumin molar ratio, with high ratios indicating a greater degree of unbound free fatty acid which is thought to be more 'toxic'.

Patients and methods

Patients

A total of 42 consecutive patients with acute myocardial infarction were studied in three separate groups.

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Patients admitted more than 12 hours from the onset of symptoms were omitted, as were 2 patients with clinical diabetes mellitus. Criteria for diagnosis of myocardial infarction were characteristic changes in blood enzymes (AAT, CPK, and LDH) and the presence of one or both of the following features: typical history; electrocardiographic abnormalities: elevation of the ST segment, with subsequent inversion of the T wave, with or without pathological Q waves.

The mean time from onset of symptoms to admission was 7.9 ± 1.1 (SEM) hours.

Procedure for repeated FFA samples

In the first group, 9 unselected consecutive male patients were studied. The mean age was 54 years (range 37 to 64). All had all three criteria for diagnosis of acute myocardial infarction. In 3 of the 9 patients there were no complications of note; in 3 there were runs of ventricular tachycardia; in 1, ventricular extrasystoles requiring lignocaine therapy; and in 2 left ventricular failure. No patients were in cardiogenic shock. Blood for free fatty acid determinations was usually taken at 2-hourly intervals from an indwelling central venous catheter for a period of 60 to 66 hours after admission (Fig. 1 and Table 1). If the catheter were blocked or required changing, the sample was omitted. The patients were allowed free access to food including sucrose but heparin or glucose infusions were withheld. A dietitian calculated the calorie intake and the carbohydrate contribution.

Sorbitol infusion

In another 4 patients, sorbitol was given as a 30 per cent solution, initially as a slow bolus intravenous injection (25 g over 2 min), followed by a continued infusion (60 ml/hr) over 4 to 12 hours.

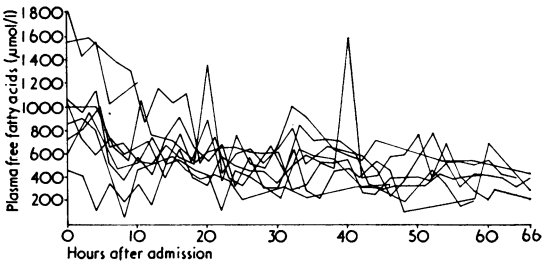

FIG. 1 *Plasma free fatty acid concentrations (μmol/l) in 2- or 4-hourly samples in 9 patients with acute myocardial infarction, 0 to 66 hours after admission to the coronary care unit. The patients were allowed free access to food but intravenous heparin or glucose were withheld. Few values exceeded 1200 μmol/l more than 10 hours after admission. There were only two unexpected 'peak' values exceeding 1200 μmol/l. The lowest initial values were found in a patient with myocardial infarction (blood creatine phosphokinase activity, 3330 units) who took 280 kcal immediately on admission. Mean values ± SEM are shown in Table 1.*

Free fatty acid values in other patients

In the other 29 consecutive patients, plasma for determination of free fatty acid and albumin was taken on three occasions: soon after admission to the coronary care unit, and before breakfast (overnight fast) on the second and third days. Samples were taken irrespective of whether or not the patients were receiving an intravenous infusion of heparin and/or 5 per cent dextrose.

TABLE 1 *Serial plasma free fatty acid concentrations in 9 patients with acute myocardial infarction*

Hours after admission	*0*	*2*	*4*	*6*	*8*	*10*	*12*	*14*	*16*	*18*	*20*	*22*
Free fatty acids (μmol/l)	1009 ±144 (9)	893 ±116 (7)	886 ±173 (7)	753 ±128 (7)	612 ±119 (6)	673 ±120 (7)	579 ±96 (7)	641 ±70 (8)	705 ±74 (8)	504 ±28 (8)	663 ±119 (8)	445 ±64 (8)
Hours after admission	*24*	*26*	*28*	*30*	*32*	*34*	*36*	*38*	*40*	*42*	*44*	*46*
Free fatty acids (μmol/l)	464 ±75 (8)	530 ±30 (7)	475 ±51 (7)	436 ±61 (8)	689 ±94 (7)	525 ±81 (8)	596 ±75 (7)	564 ±40 (6)	664 ±136 (8)	403 ±54 (6)	414 ±61 (7)	388 ±53 (6)
Hours after admission	*48*	*50*	*52*	*54*	*56*	*58*	*60*	*62*	*64*	*66*		
Free fatty acids (μmol/l)	338 ±71 (6)	517 ±133 (3)	494 ±76 (5)	490 ±76 (5)	382 ±66 (5)	387 ±66 (6)	490 ±73 (4)	373 ±37 (3)	375 ±25 (2)	350 ±46 (4)		

Mean values ± SEM (number of patients studied).
For individual values see Fig. 1.

Analytical procedures

Plasma was separated immediately after sampling and frozen until assayed for free fatty acid by the method of Dole and Meinertz (1960). Plasma albumin was measured by the method of Miyada *et al.* (1972).

Results

Plasma free fatty acid concentrations in 9 patients studied in detail (Fig. 1 and Table 1)

Out of a total of 229 blood samples taken at 2- or 4-hourly intervals, only 10 exceeded 1200 μmol/l though a further 14 fell between 1000 and 1200 μmol/l. Sixteen of the 24 values exceeding 1000 μmol/l occurred in the same 4 patients and fell within the first 10 hours of admission. After the first 10 hours only 7 values exceeded 1000 μmol/l and of these there were only 2 sudden unexpected 'peaks'.

An example of the effect of oral calorie intake on the plasma free fatty acid pattern is shown in Fig. 2. Intake of calories tended to be followed by a decrease of plasma free fatty acids, which were higher during the fasting period at night.

Taking the 9 patients as a group, their average daily calorie intake rose from 395 kcal on the first day, to 833 on the second, to 1130 on the third day (Table 2). On each day an average of 50 per cent of the calories were derived from carbohydrates. However, only on the first day was there a significant decrease of plasma free fatty acid values after every intake of calories exceeding 90 kcal (378 kJ); whereas on the second and third days, only calories at breakfast were followed by a significant reduction of plasma free fatty acid values.

Sorbitol in 4 patients

In 3 patients the circulating glucose concentration increased by over 60 mg/100 ml with the rise starting about 30 minutes after the sorbitol bolus, and the circulating concentration of free fatty acids decreased by about 50 per cent for about 2 hours; thereafter neither the free fatty acid values fell nor did the blood sugar rise with the rate of infusion given. In a fourth patient with cardiogenic shock sorbitol did not increase blood glucose concentrations, nor did blood free fatty acid concentrations fall. In the other 3 patients, the increase of blood sugar was probably as a result of conversion of sorbitol to fructose to glucose in the liver.

Studies on 29 consecutive patients

In 15 patients receiving heparin and glucose intravenously and in 7 receiving only glucose, only small changes were seen over the first 3 days in the early morning fasting free fatty acid values which varied from 780 ± 82 (n = 22) μmol/l on the first day to 653 ± 58 (n = 19) μmol/l on the third day. The mean plasma free fatty acid values (all values for days 1 to 3 grouped) in patients with infusions of intravenous 5 per cent glucose were 603 ± 55

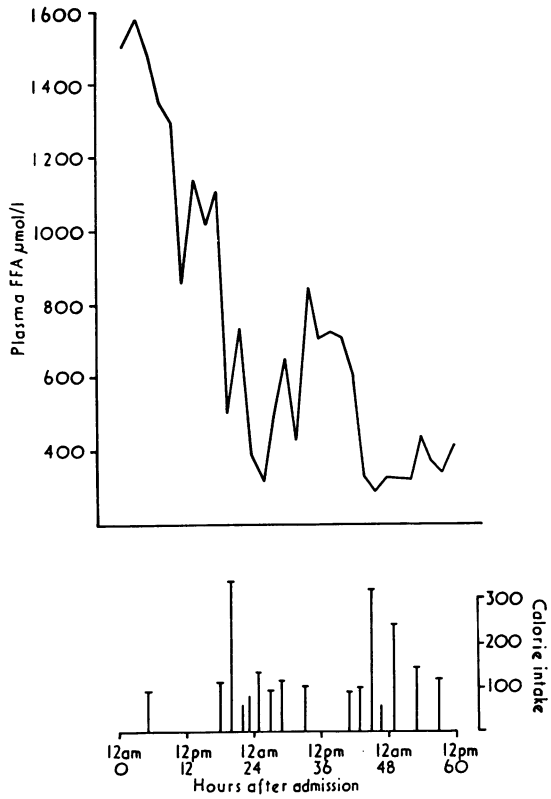

FIG. 2 *Relation between oral calorie intake and plasma free fatty acid values in a 52-year-old patient with uncomplicated acute inferior myocardial infarction. The patient was selected as having a high initial free fatty acid value. Note that on the first day (12 a.m.–12 p.m.) oral feeding was associated with a fall in free fatty acid values; on the second day (12 to 36 hours after admission), 120 kcal (504 kJ) at 6 a.m. and 331 kcal (1340 kJ) at 8 a.m. were followed by a fall of plasma free fatty acid values; thereafter, there was no consistent effect of oral calories until breakfast on the third day (36 to 60 hours after admission in this case) when 90 kcal (378 kJ) were followed by a pronounced fall in free fatty acid values; thereafter again no consistent effect. This pattern is typical for the group as a whole (see Table 1 and Results).*

TABLE 2 *Average daily calorie intake and effect on plasma free fatty acid values in 9 patients with acute myocardial infarction fed* ad libitum

	Average calorie intake kcal per day	*% calories from carbohydrate*	** Change in plasma free fatty acids (μmol/l) Change per intake of 90 kcal or more*	*Change in plasma free fatty acids as result of breakfast alone (μmol/l)*
Day 1	395 ± 96 (9)	49%	−145 ± 39 (17)	
Day 2	833 ± 160 (8)	50%	−4 ± 44 (23)	−248 ± 86 (7)
Day 3	1130 ± 149 (8)	49%	−23 ± 45 (23)	−206 ± 50 (7)

* Change in plasma free fatty acids calculated from comparison of value in 2-hourly sample before calorie intake, compared with next sample after calorie intake. Mean values ± SEM for (number of observations).
1 kcal = 4.2 kJ.

μmol/l (n = 43), with intravenous glucose + heparin (average daily dose 11,000 to 12,000 units), 738 ± 74 μmol/l (n = 36); and with intravenous heparin alone, 1558 ± 307 μmol/l (n = 8). In patients with infusions of neither glucose nor heparin, mean free fatty acid values were 740 ± 51 μmol/l (n = 20). Though free fatty acid values with glucose + heparin differed significantly from those with heparin only ($P < 0.02$), allocation of patients to the heparin or heparin + glucose groups was not randomized and further studies are required to show whether glucose has an effect on heparin-induced increase of plasma free fatty acid values. The mean plasma albumin value fell from 41 ± 2 g/l (n = 16) on the first day to 38 ± 3 g/l (n = 13) on the second day to 36 ± 2 g/l (n = 17) on the third day. These values probably reflect changes in the plasma volume (Sedziwy, Thomas, and Shillingford, 1968). The free fatty acid : albumin molar ratio was virtually steady (first day 1.5, second day 1.5, third day 1.2). In rat hearts, values of 3 : 1 to 5 : 1 are required for arrhythmogenicity (Willebrands *et al.*, 1973).

Discussion

Several lines of evidence suggest that carbohydrate calories, taken orally or intravenously, diminish circulating free fatty acid values in patients with acute myocardial infarction. In our study ingestion of calories, taken *ad libitum*, decreased plasma free fatty acid concentrations throughout the first day and thereafter decreased high pre-breakfast values. The major single source of these calories was carbohydrate (about 50% of total calories), and plasma free fatty acids fell by a mean of 145 μmol/l for each oral intake of 90 kcal (378 kJ) or more. Intravenous sorbitol was an effective antilipolytic agent in 3 non-shocked patients. Gupta *et al.* (1969) showed that 25 g glucose given intravenously on the first day after acute myocardial infarction reduced free fatty acid values to within normal range within 2 hours. Allison, Chamberlain, and Hinton (1969) found a similar decrease of free fatty acids in non-shocked patients but a lesser fall in shocked patients, probably because of decreased insulin release. Oliver, Rowe, and Vetter (1972) found that the intravenous infusion of 5 per cent dextrose together with 5 i.u. insulin or an infusion of 10 per cent dextrose over 2 to 3 hours brought down plasma free fatty acid values in patients with acute myocardial infarction. Though such relatively small amounts of intravenous or oral carbohydrate can decrease circulating free fatty acids in patients with acute myocardial infarction, in patients developing shock the administration of insulin may also be needed. Other means of reducing plasma free fatty acids are by infusion of glucose, insulin, and potassium or by nicotinic acid analogues such as 'ronicol' (β-pyridyl-carbinol) (Oliver *et al.*, 1972; Rowe *et al.*, 1973).

If the currently available animal experimental work (Opie, 1972) could be extrapolated to man, the effect of early carbohydrate calorie intake such as oral glucose or sucrose or of intravenous glucose or sorbitol in reducing circulating free fatty acid values and increasing the blood sugar, would be expected to have a helpful rather than a harmful effect on the outcome of myocardial infarction in man. Our studies do not provide direct evidence for or against the hypothesis that high free fatty acid values may be undesirable in early acute myocardial infarction, but show that dietary antilipolytic therapy requires consideration for further investigation. As it may be during the first few hours after acute infarction that high free fatty acid values are least desirable, the effect of oral calories during this

early period requires investigation, with special reference to the possible difficulty in the administration of oral calories to patients with severe complications who are those likely to have highest blood free fatty acid values according to Oliver *et al.* (1968) and Gupta *et al.* (1969).

Adequate evaluation of the possible benefit of such dietary antilipolytic procedures awaits the detailed results of further human and animal studies (e.g. Rowe, Neilson, and Oliver, 1974; de Leiris, Opie, and Lubbe, 1975; Opie and Lubbe, 1975) to clarify further the relation between circulating free fatty acids and complications of acute myocardial infarction. In the meantime we would argue against the traditional concept that patients with acute myocardial infarction should be semi-starved at the start of their illness, and suggest that such patients should be encouraged (but not forced) to eat or drink carbohydrate-rich foods.

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