Duration and results of manipulation in 20 consecutive patients

Case No	Manipulation time (minutes)	Screening time (minutes)	Result
1	6·5	4·5	Normal
2	4·5	3·0	Coeliac disease
3	4·75	3·5	Normal
4	4·5	2·5	Coeliac disease
5	9·0	4·25	Normal
6	3·5	2·25	Normal
7	8·5	5·25	*
8	12·0	4·75	Normal
9	9·75	4·5	Normal
10	8·0	4·25	Normal
11	1·5	0·75	Normal
12	7·5	3·75	Normal
13	14·0	6·5	Coeliac disease
14	13·0	6·0	Normal
15	3·5	2·0	Normal
16	7·5	4·75	Normal
17	4·75	2·5	Normal
18	7·0	5·0	Normal
19	7·5	5·0	Normal
20	4·0	2·75	Coeliac disease

*Capsule failed to pass through pylorus because stomach was axially rotated.

flexure in 20 cases varied between 1·5 and 14 (mean 7·4) minutes. The average screening time was four minutes. In only one patient (case 10) had the capsule already passed through the pylorus when he was first screened in the *x* ray department. In all other patients the capsule was near the pylorus when they were first screened.

Comment

Fluoroscopy, though important to the procedure, is used intermittently and kept to a minimum. The technique is rapid, simple, and much less uncomfortable for the patient than other methods of placing capsules.

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Self poisoning with enalapril

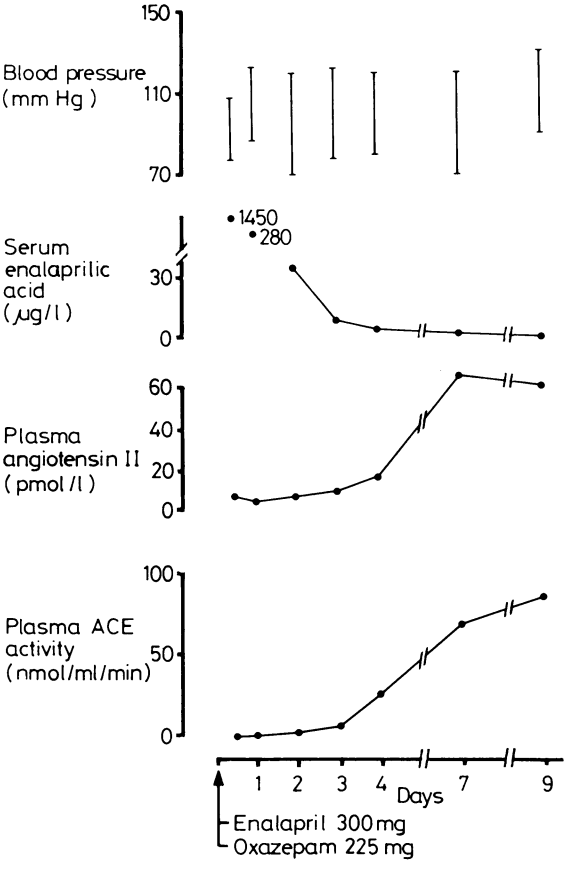
Enalapril (MK-421; *N*-(1-ethoxycarbonyl-3-phenylpropyl)-L-alanyl-L-proline hydrogen maleate) is an angiotensin converting enzyme inhibitor[1] that is useful in managing patients with hypertension and congestive heart failure refractory to conventional treatment.[2 3] It is a prodrug that must be hydrolysed in vivo to its parent diacid compound enalaprilic acid (MK-422), which is biologically effective. Long term blockade of the renin angiotensin system with this agent is usually well tolerated, but no information has been available on the effects of acute overdosage. We report on a patient who tried to commit suicide by ingesting a large dose of both enalapril and oxazepam, a benzodiazepine.

Case report

The patient was a 46 year old woman with severe essential hypertension and a history of right side cerebrovascular accident. Her blood pressure had been well controlled with enalapril (20 mg twice daily) and chlorthalidone (100 mg once daily) for two years when she attempted to commit suicide by ingesting 300 mg enalapril and 225 mg oxazepam. On admission four hours later she was stuporous but had not developed respiratory distress. Blood pressure was 100/60 mm Hg and heart rate 80 beats/minute. During the subsequent hours blood pressure oscillated around 80-100/50-80 mm Hg and consciousness progressively improved. Occasional ventricular premature contractions were recorded, but her pulse rate showed no tendency to accelerate. After infusion of 2000 ml sodium chloride 0·9% and 250 ml plasma intravenous blood pressure rose to 110-125/70-85 mm Hg, within the first 24 hours after admission.

She was discharged after three weeks' uneventful observation; her blood pressure still had not reached hypertensive values, though no antihypertensive treatment had been given. Ten days later enalapril and chlorthalidone had to be restarted. Laboratory profiles remained normal throughout the month after drug overdosage.

The figure shows the time course of the changes in the serum concentration of enalaprilic acid, plasma angiotensin II concentration, and plasma angiotensin converting enzyme activity after the attempted suicide. Plasma angiotensin II and serum enalaprilic acid concentrations were measured by radioimmunoassay and plasma angiotensin converting enzyme activity by a radioenzymatic method.[3 4] Ten hours after ingestion of 300 mg enalapril the serum concentration of enalaprilic acid had reached 1450 μg/l and plasma angiotensin converting enzyme activity had been completely suppressed. At the same time the serum concentration of enalapril was 50 μg/l. This was estimated as the difference between concentrations of enalaprilic acid before and after in vitro hydrolysis of the residual enalapril contained in the sample tested. Only from her fourth day in hospital did the plasma angiotensin concentration start to increase and plasma angiotensin converting enzyme to resume its activity. Blood pressure remained normal despite the unblocked renin angiotensin system.



Changes in blood pressure, serum concentration of enalaprilic acid, plasma angiotensin II concentration, and plasma angiotensin converting enzyme (ACE) activity after ingestion of 300 mg enalapril and 225 mg oxazepam.
Conversion: SI to traditional units—Plasma angiotensin II: 1 pmol/l ≈ 1 pg/ml.

Comment

Enalapril is a potent long acting angiotensin converting enzyme inhibitor that has to be hydrolysed in vivo to its active metabolite enalaprilic acid. In our patient serum of enalaprilic acid concentrations 10 hours after ingestion of 300 mg enalapril were over 100 times higher than necessary to inhibit angiotensin converting enzyme.[4] The capacity to hydrolyse enalapril was not exceeded because at the same time there was little intact drug in the serum.

Overdosage with enalapril and oxazepam did not cause any serious complications. The hypotensive episode shortly after overdosage was well tolerated and easily reversed by supportive infusion of fluid.

The blood pressure returned to hypertensive values only three weeks after recovery of an intact renin angiotensin system. This is surprising even though it is known that continuous control of blood pressure can be achieved despite intermittent resumption of normal angiotensin converting enzyme activity.[5]

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Prognostic importance of hyperglycaemia induced by stress after acute myocardial infarction

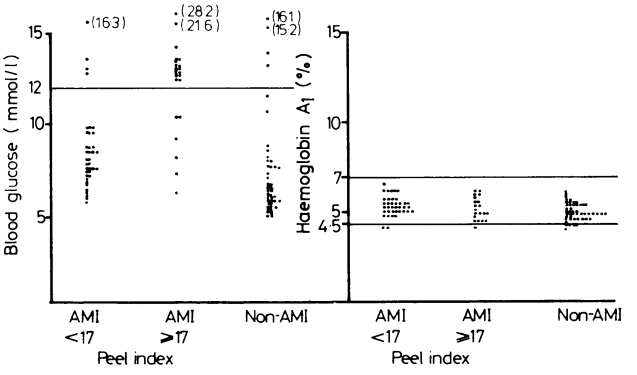
Transient hyperglycaemia is a recognised finding during acute myocardial infarction and is considered to be related to stress. On clinical signs alone hyperglycaemia induced by stress cannot be differentiated from undiagnosed diabetes mellitus. In this study we measured haemoglobin A_1 concentrations to differentiate between the two conditions. Hyperglycaemia induced by stress in acute myocardial infarction was then related to prognosis using the coronary risk index of Peel *et al*[1] (a prognostic index for grading the severity of infarction based on sex, age, ischaemic history, shock, heart failure, and electrocardiographic changes; a score of ≥ 17 is associated with a 50% risk of death).

Patients, methods, and results

We studied 110 patients admitted to hospital with suspected acute myocardial infarction. They were examined on admission and note made of pulse rate, blood pressure, cardiac rhythm, and the presence or absence of shock or cardiac failure. The examination was repeated on days 1, 2, and 10 after admission. Blood glucose concentrations were measured on admission and after fasting on days 1 to 5. Haemoglobin A_1 concentrations were measured on days 1 and 3. All patients who had hyperglycaemia and survived, other than those known to have diabetes, were reviewed three months later, when haemoglobin A_1 concentrations were measured. Glucose tolerance tests were also performed at that time by measuring blood glucose concentrations on fasting and one and two hours after ingestion of 75 g glucose.

In the assay of haemoglobin A_1 concentrations red cells were diluted in a ratio of 1:10 with physiological saline and incubated overnight before formation of the haemolysate. The assay was then performed using a Biorad column test kit (catalogue No 191-7001). Blood samples taken from 40 healthy laboratory staff two hours after a meal gave a normal range of 4·5-7%; in all samples the glucose concentrations were lower than 7·3 mmol/l (132 mg/100 ml).

Acute myocardial infarction, defined according to criteria of the World Health Organisation,[2] was confirmed in 61 patients, 21 of whom (34%) had hyperglycaemia compared with four of the 49 (8%) without acute myocardial infarction ($\chi^2=9·2$; df=1; $p<0·01$) (figure). Only one patient with acute myocardial infarction had a raised haemoglobin A_1 concentration (11%) and died during the acute phase. Fourteen patients died during admission and a further four during the follow up, giving a total death rate of 30%. Hyperglycaemia was then related to prognosis using the Peel index. The death rates after acute myocardial infarction were 57% (12/21) in patients with hyperglycaemia induced by stress and 15% (6/40) in those without ($\chi^2=9·8$; df=1; $p<0·01$). A Peel index of ≥ 17 was found in 17 out of 21 patients (80%) with and six out of 40 patients (15%) without hyperglycaemia ($\chi^2=22·8$; df=1; $p<0·001$). Among 49 patients who did not suffer acute myocardial infarction four had hyperglycaemia induced by stress; all four presented with acute left ventricular failure. One died during follow up. Ultimately haemoglobin A_1 concentrations were measured and glucose tolerance tested in 12 patients who had hyperglycaemia induced by stress and survived. The results of both tests were normal in 10 patients and indicative of diabetes in two, one of whom had a haemoglobin A_1 concentration of 7·7%.



Haemoglobin A_1 and blood glucose concentrations in patients on admission with and without acute myocardial infarction (AMI). Patients with Peel index ≥ 17 are compared with those with Peel index < 17 ($\chi^2=9·2$; df=1; $p<0·01$). Horizontal lines indicate upper limit of normal glucose concentration and normal range of haemoglobin A_1 concentration. The four patients without AMI whose blood glucose concentrations were above the normal range had left ventricular failure.

Conversion: SI to traditional units—Glucose: 1 mmol/l $\approx$ 18 mg/100 ml.

Comment

Our study showed that hyperglycaemia is common after acute myocardial infarction whereas high haemoglobin A_1 concentrations are less common. Accordingly, routine measurement of haemoglobin A_1 concentrations in patients thought to have hyperglycaemia induced by stress is unlikely to be helpful despite a previous suggestion that it is of value for early interpretation of hyperglycaemia after acute myocardial infarction.[3] We also showed that hyperglycaemia induced by stress is associated with poor prognosis in patients who have had acute myocardial infarction. Follow up of such patients suggested that hyperglycaemia induced by stress is a temporary phenomenon in patients with otherwise normal carbohydrate tolerance, contrary to previous findings.[4] We conclude that hyperglycaemia induced by stress should be considered to be a crude prognostic marker in acute myocardial infarction indicating poor prognosis and high mortality.

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