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Effect of intravenous infusion of insulin in diabetics with acute myocardial infarction

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Abstract

Diabetes mellitus is associated with a high mortality after myocardial infarction. To see whether this may be decreased by improved diabetic control the effect of an insulin infusion regimen was studied in patients with acute myocardial infarction.

From April 1982 to April 1983, 33 diabetics were admitted with acute myocardial infarction. Those being treated with diet alone or oral hypoglycaemic drugs continued with this unless control was poor, when they were changed to a "sliding scale" regimen of subcutaneous insulin injections thrice daily. Those already receiving insulin were maintained on thrice daily subcutaneous injections. From April 1983 to April 1984, 29 diabetics had acute myocardial infarction. Those receiving treatment with oral hypoglycaemic drugs or insulin were changed to continuous intravenous infusion of insulin, the aim being to maintain the blood glucose concentration at 4-7 mmol/l (72-126 mg/100 ml). Those being treated with diet alone continued with this if blood glucose concentrations were acceptable. Total mortality fell from 42% in the first year to 17% in the second ($p < 0.05$). Over the same period mortality among non-diabetic patients with myocardial infarction did not change significantly. There was a significant fall in cardiac arrhythmias (expressed as the percentage of patients in whom arrhythmias were recorded) from 42% to 17% ($p < 0.05$). The most significant fall in the incidence of complications occurred in those who had been receiving oral hypoglycaemic drugs on entry to the study (87% to 50%, $p < 0.05$).

This study found an improvement in outcome associated with a regimen of continuous insulin infusion in diabetics with acute myocardial infarction. This may have been related to a fall in the incidence of cardiac arrhythmias.

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Introduction

Acute myocardial infarction is associated with a higher mortality in diabetics than non-diabetics.[1] In our unit in the year before this study diabetics with acute myocardial infarction had a mortality of 37%, compared with a mortality of 12% in non-diabetics. This may be due to more extensive coronary atherosclerosis,[2] greater impairment of left ventricular function,[3-5] and the effects of autonomic neuropathy (tachycardia, impaired perception of pain). Metabolic changes that occur at the time of myocardial infarction, which are more pronounced in diabetics, may also be deleterious and include the release of catecholamines[6] and corticosteroids[7] (inhibiting the action of insulin and impairing the supply of energy to the myocardium) and of free fatty acids[8] (predisposing to arrhythmias[9] and increasing myocardial consumption of oxygen).[10]

This high mortality might be decreased by improved diabetic control in the period immediately after infarction. The use of continuous intravenous infusion of insulin is simple and facilitates metabolic control.[11] This study describes the effects of changing to this method of diabetic control in established diabetics with acute myocardial infarction.

Patients and methods

From April 1982 to March 1983, 33 diabetics were admitted to the coronary care unit with acute myocardial infarction (group 1). Myocardial infarction was diagnosed when chest pain was present and electrocardiography and enzyme activity indicated infarction. All subjects were known diabetics before admission. Those being treated with diet alone or receiving oral hypoglycaemic drugs continued with this treatment unless control was poor, when they were changed to multiple subcutaneous injections of soluble insulin. Those already receiving insulin were maintained on subcutaneous injections administered before each main meal.

From April 1983 to March 1984, 29 diabetics were admitted with acute myocardial infarction (group 2). Those receiving oral hypo-

glycaemic drugs or insulin were changed to continuous intravenous infusion of insulin. Blood glucose concentration was monitored by Ames glucometer hourly for the first four hours, four hourly for the next 24 hours, and before meals on days 2 and 3. Actrapid MC insulin was given according to the regimen shown in table I to maintain blood glucose concentrations at 4-7 mmol/l (72-126 mg/100 ml). On day 4 treatment was changed to Actrapid insulin administered subcutaneously before each main meal. Patients being treated with diet alone continued with this unless control was poor, when they were changed to intravenous insulin.

TABLE I—*Doses of Actrapid MC insulin in 5% dextrose given at various blood glucose concentrations*

Blood glucose (mmol/l):	<4	4-	8-	12-	22
Insulin (U/h):	0	½	1	2	4

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

Patients who died before intravenous treatment could be started were not included in the study. Mortality figures pertain to the period spent in hospital, on average two weeks after the myocardial infarction. Complications were noted only if they required treatment—that is, heart failure, diagnosed clinically or radiologically, requiring a diuretic; and arrhythmias, shown by electrocardiography, requiring specific antiarrhythmic treatment.

Statistical methods—Changes in mortality and complications were assessed by χ^2 test with Yates's correction. Relative risks were assessed by McNemar's test or the binomial test, as appropriate.

Results

Table II gives the characteristics of the 62 patients. There was no significant difference between the two groups in age, sex distribution, site of myocardial infarction, incidence of previous myocardial infarction, duration of diabetes, incidence of hypertension, or cigarette smoking. There was no difference in the cardiac drugs taken before admission or in the mean plasma glucose concentration on admission. Table III lists the treatments given.

Table IV shows the results. There was a significant difference in total mortality between the two groups (42% in group 1 (1982-3) *v* 17% in group 2 (1983-4), $p < 0.05$).

There was no change in mortality among non-diabetic subjects with myocardial infarction during the two years of the study (14% and 13%). The incidence of cardiac arrhythmias requiring treatment fell significantly, from 42% to 17% ($p < 0.05$). When the two major complications of myocardial infarction were considered together (heart failure and arrhythmias) there was no significant change in those patients who had received either diet alone or insulin before admission.

TABLE II—*Characteristics of patients in the two groups*

	Group 1	Group 2
No of patients	33	29
Mean age (years)	65	64
No (%) of men	20 (61)	18 (62)
Mean blood glucose on admission (mmol/l)	16·4	17·8
No (%) of patients with inferior infarcts	19 (58)	18 (62)
No (%) of patients with previous infarcts	12 (36)	9 (31)
Duration of diabetes (years)	8·8	9·9
No (%) of patients with hypertension	3 (9)	5 (17)
No (%) of current smokers	1 (3)	2 (7)

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

TABLE III—*Treatments prescribed on entry to study*

Treatment on admission	Group 1	Group 2
Diet alone	10 continued diet 2 subcutaneous insulin	10 continued diet 1 intravenous insulin
Oral hypoglycaemic drugs	8 continued 7 subcutaneous insulin	All insulin infusion (12 patients)
Insulin	All subcutaneous insulin (6 patients)	All insulin infusion (6 patients)

TABLE IV—*Results of treatments prescribed. Figures are numbers (%) of patients*

	Total	Patients treated by diet	Patients treated with oral hypoglycaemic drugs	Patients treated with insulin
Mortality:				
Group 1 (n = 33)	14 (42)	4 (33)	5 (33)	5 (83)
Group 2 (n = 29)	5 (17)*	3 (27)	1 (8)	1 (16)
Complications (heart failure, arrhythmias):				
Group 1	26 (79)	9 (75)	13 (87)	5 (83)
Group 2	15 (52)**	5 (45)	6 (50)*	4 (67)
Arrhythmias:				
Group 1	14 (42)			
Group 2	5 (17)*			

*$p < 0.05$; **$p < 0.01$.

TABLE V—*Mortality and relative risk in the two groups of diabetics compared with two groups of non-diabetics with myocardial infarction matched for age*

	Mortality (%)		Relative risk compared with non-diabetics
	In diabetics	In non-diabetics	
Group 1	42	16	5·5 ($p < 0.05$)
Group 2	17	13	1·3 ($p < 0.1$)

In those receiving oral hypoglycaemic drugs the occurrence of complications fell significantly (87% to 50%, $p < 0.05$).

Table V shows results expressed as age matched mortality and relative risk for the two groups. This confirms that the diabetics in group 1 were at a greater risk than non-diabetics matched for age. The diabetics in group 2 had a similar risk to non-diabetics. Results over the past year (April 1984 to April 1985) showed a continuing low mortality among diabetics with acute myocardial infarction (5/35, 14%) compared with a mortality in non-diabetics of 11%.

Discussion

As well as having an increased incidence of coronary artery disease, diabetics who suffer a myocardial infarction have a higher mortality than non-diabetic subjects. This may be related to features peculiar to diabetics, including more extensive atherosclerosis, affecting particularly the smaller coronary arteries, compared with disease predominantly affecting the large vessels in non-diabetics. A specific diabetic cardiomyopathy,[5] by impairing left ventricular function, may be disadvantageous. Autonomic neuropathy found in some diabetics may cause tachycardia, hence increasing cardiac workload. The diminished perception of pain in such patients may be deleterious, leading to longer delays before they seek medical help during acute myocardial infarction.

Diabetics are prone to certain metabolic changes at the time of infarction which may be expected to benefit from improved diabetic control. As in other acutely stressful conditions there is an increased output of catecholamines[6] and corticosteroids,[7] which inhibit the action of insulin and hence impair the myocardial uptake of glucose (the main source of energy for ischaemic myocardium). An increased output of free fatty acids[8] (which would be inhibited by insulin) may be associated with increased myocardial consumption of oxygen[10] and a predisposition to arrhythmias.[9]

The experimental use of glucose-insulin-potassium infusions in animals has shown evidence of reduced infarct size and improved myocardial metabolism.[12]

Continuous intravenous infusion of insulin is a simple and effective way of controlling diabetes in stressful conditions, including acute myocardial infarction.[11] Our study has shown a significant fall in mortality, from 42% to 17%, with the change to infusion of insulin. The mortality in group 1 was similar to that in other studies of diabetics with acute myocardial infarction. The fall is unlikely to have been caused by other changes in treatment as the mortality of non-diabetic patients was constant over the two years of the study. There were no other major

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changes in the treatment policy of the cardiac control unit during this period.

The fall in mortality was confined to those patients who had previously received insulin or oral hypoglycaemic drugs and did not occur in the group treated by diet. The reduction in the incidence of major complications was significant only in the group who had received oral hypoglycaemic drugs before admission. Oral hypoglycaemic drugs have several potentially deleterious effects in patients with coronary heart disease. Sulphonylureas have a positive inotropic action, which is generally disadvantageous in acute myocardial infarction, leading to increased myocardial consumption of oxygen and possibly increased infarct size. These agents may be harmful in myocardial infarction, and a change to insulin could therefore be of benefit. Biguanides are associated with the development of acidosis in stressful illnesses, including myocardial infarction, but none of our control patients showed evidence of this metabolic upset. Furthermore, a study by the University Group Diabetes Program found an increased cardiovascular mortality in patients receiving oral hypoglycaemic drugs.[13] Although the design and conclusion of this study were criticised,[14] a later review concluded that there was evidence of harmful effects from these agents.[15]

Our results differ from a recent study using a similar regimen in diabetics suffering from acute myocardial infarction. Gwilt *et al* found no improvement in mortality after changing to continuous intravenous infusion of insulin.[16] The reasons for this difference are not clear. Our patients were of similar age and sex distribution and had similar blood glucose concentrations on admission, but they had a higher incidence of previous myocardial infarction.

Because of our mobile cardiac unit patients are admitted to hospital more rapidly than in units without this facility. It may be that, to be effective, the infusion of insulin has to be begun as early as possible in the course of acute myocardial infarction; this aspect requires further study.

In conclusion, we have shown a fall in mortality and complications in diabetics treated with continuous intravenous infusion of insulin after an acute myocardial infarction. The effect on complications appears to be most noticeable in those who received oral hypoglycaemic drugs before admission. This was not a controlled trial, but such a trial is now under way. Nevertheless, as an observation of the effects of a change in treatment this study would indicate that such treatment should be considered in all diabetics suffering acute myocardial infarction.

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Early gastric cancer: the case for long term surveillance

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Abstract

Thirty five patients with early gastric cancer have been treated at the Bristol Royal Infirmary since 1965. The number of cases diagnosed has doubled in the last 10 years. Epigastric pain (74%), loss of weight (63%), and gastrointestinal bleeding (43%) were the most common presenting symptoms, with a median length of history of 12 months (range five days to 72 months). Life table survival curves showed a crude five year survival of 71% (age adjusted 92%) and a crude 10 year survival of 63% (age adjusted 85%). Sixteen patients have been followed up clinically, endoscopically, and by scintigraphy with technetium-99m *p*-butyl iminodiacetic acid to assess the risk of recurrent disease. Of seven patients with pronounced bile reflux, two had moderate dysplasia of the gastric remnant, and one patient was found to have developed a metachronous tumour nine years after surgery.

Partial resection seems to be the best choice of treatment for early gastric cancer, giving good functional results. Consideration should, however, be given to Roux en Y diversion, and long term surveillance of the gastric remnant is recommended.

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Introduction

In 1938 Saeki identified a subgroup of patients with gastric cancer of limited depth of invasion who had a 90% five year survival.[1] In 1962 the Japanese Endoscopic Society defined this adenocarcinoma confined to the gastric mucosa or submucosa with or without lymph node metastases as "early gastric cancer."[2] In recent years the prevalence of early gastric cancer in the Western world has risen. Between 1960 and 1969 less than 1%

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