PREVALENCE AND RISKS OF STRESS HYPERGLYCEMIA AND UNDIAGNOSED DIABETES MELLITUS IN PATIENTS WITH ACUTE MYOCARDIAL INFARCTION

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ABSTRACT

The prevalence of hyperglycemia and undiagnosed diabetes was assessed in 150 patients (without known diabetes) admitted to coronary care unit with cofirmed acute myocardial infarction (AMI).

Admission plasma glucose (APG) concentration was measured for all cases and glycosylated haemoglobin (HbAlc) concentration was measured in patients with hyperglycemia. With the use of APG level of > 144 mg/dl and an HbA1^c > 8.5% as a combined diagnostic criteria, 5.3% of patients (8/150) had previously unrecognised diabetes. 13.3% of patients with AMI had hyperglycemia without previous glucose intolerance as evidenced by normal AbA1^c level. Hyperglycemia alone, without an elevated HbA1^c level, is an indication of "stress" and is not diagnostic of diabetes. HbA1^c measurment is useful for early and accurate interpertation of hyperglycemia following AMI.

Four out of 20 patints with stress hyprglycemia died with cardiogenic shock.

APG was higher in non-survivors than in survivors (257.7± 31.3 VS 174 ± 106.7 P < 0.001).

Of the 16 survived patients with hyperglycemia and AMI 9 developed heart failure. APG was significantly higher in patients with heart failure than compensated patients (216.6 ± 30.3 VS 155.7 ± 13.1 P < 0.001).

There was a correlation between APG and infarct size as estimated by creatine kinase enzyme activity in the 20 patients with stress hyperglycemia.

AIM OF WORK

Hyperglycemia is a common finding during acute myocardial infarction (AMI). Hyperglycemia may result from stess or may be due to pre-existing undiagnosed diabetes mellitus (Oswald et al., 1986). Soler (1981) suggested that determination of glycosylated haemoglobin (HbA_{IC}) concentration could be used to separate these two conditions. A raised plasma glucose level together with an elevated HbA_{IC} cocentration indicates previously unrecognized diabetes.

Some authors have shown that hyperglycemia is a temporary phenomenon induced by stress (Bellodi et al., 1989), while other investigators indicated that previously undiagnosed diabetes is more likely than stress - induced - hyperglycemia (Madsen et al., 1986).

The reasons for excessive mortality in diabetic patients with AMI remain undetermincd. A relation has been described in patients with AMI between hyperglycemia on admission and the development of cardiogenic shock independent of the state of previous glucose intolerance (Oswald et al., 1986).

The aim of this study is to assess the prevalence of hyperglycemia and undiagenosed diabetes, and to differentiate between stress-and diabetes-induced hyperglycemia in patients with AMI.

This study also, assesses the prognostic value of hyperngIycemia and its relation to the complications of AMI in non-diabetic patients.

MATERIAL AND METHODS

The study group consisted of 150 patients, without known diabetes mellitus, admitted to Kasr-El-Eini intensive care unit (ICU) with acute myocardial infarction.

AMI was defined according to criteria of World Health Organization (1976). On admission before any drug administration or glucose infusion, blood samples were taken to determine plasma glucose and creatine kinase enzyme (CK) andevery 6 hours for 48 hours-to assess CK enzyme.

Patients with an admission plasma glucose concentration (APG) > 144/100 ml had blood drawn for measurement of stable glycosylated haemoglobin by isoelectric focussing method (Mortensen, 1980).

Samples for HbA1c determination were taken into sodium heparin tubes and stores at 4°C for up to 7 days.

No patients with hyperglycemia was given insulin. Analysis of patients considered : age and sex, history of previous myocardial infarction, hypertension or smoking, ventricular arrythmias detected hy electrocardiographic monitoring, development of left ventricular failure (LVF) or cardiogenic shock.
Killip class was assigned as :
Killip I : no clinical signs of heart failure;
Killip II: bibasilar rales and auscultatory third heart sound, killip III, acute pulmonary edma and killip IV, cardiogenic shock with systolic blood pressure <90 mmHg associated with oliguria.

HbAlc concentration was measured in 10 non-diabetic control subjects without AMI. Before discharge from the intensive care unit, fasting and post-prandial plasma glucose were measured for all patients with admission hyperglycemia.

RESULTS

The normal range of HbAlc in our assay was 4.5 to 7% of total haemoglobin.

Patients with HbAlc concentration > 8.5% were considered to have undiagnosed diabetes (Oswald et al., 1984).

On the basis of recent recommendations regarding the application of the WHO criteria (Jarrett, 1983) for diagnosing diabetes in symptomless subjects, both a fasting plasma glucose ≥144 mg/dL and 2hr plasma glucose ≥198 mg/dL were required for diagnosis of diabetes.

Patients with known diabetes were excluded from this study.

8 patients had APG >144 mg/dL and HbA_{1c} concentration >8.5% which is indicative of prevalence of undiagnosed diabetes in our group of AMI patients was 5.3% (8/150).

20 patients with AMI had APG > 144 mg/dL and a concentration of HbA1c within the normal range (Table 1). Such hyperglycemia was temporary as before discharge from ICU oral glucose (75 g) tolerance test perfomed after overnight fast in these 20 patients showed a normal fasting and post-prandial plasma

glucose. The prevalence of stress hyperglycemia in this group of AMI patients was 13.3% (20/150).

There was a significant relation between APG and peak CK enzyme activity in the 20 myocardial infarction patients and stress hyperglycemia ($r = 0.27$, $P < 0.001$), (Fig. 1), however there was no correlation between APG and HbA1c levels in this group of patients.

Four patients out of 20 patients with stress hyperglycemia died with cardiogenic shock. Mortality was not related to the development of ventricular arrythmias, age, thrombolytic therapy, whereas it increased in presence of heart failure (Killip Class).

APG and CK enzyme were significantly higher in non survivors than in survivors (Table 3).

The prevalence of patients with signs of heart failure in the 16 surviving patients with stress hyperglycemia was 56.2% (9/16). APG was higher in patients with heart failure compared to compensated patients (Table 4).

Table 1 : Summary of the laboratory data of 150 patients with AMI

Normoglycemia	No. of cases 122/150 (81.4%)
Hyperglycemia (APG > 144 mg/dL)	28 (18.6%)
Hyperglycemia with HbA_{1c} < 8%	(undiagnosed diabetes) 8/150 (5.3%)
Hyperglycemia with HbA_{1c} > 8%	(stress hyperglycemia) 20/150 (13.3%)

Table 2 : APG level in the 20 cases with stress hyperglycemia .

APG (mg/dL)	No. of cases
144 - 198	11
198 - 250	4
Above 250	5

Table 3 : Comparison of APG and CK enzyme between survivors and non-survivors of 20 patients with AMI and stress hyperglycemia .

	Suvivors (16)	Non-suvivors (4)	P value
C.K. (U/L)	452.3±248.9	942.5±267.9	< 0.001
APG (mg/100 ml)	174.6±106.7	257.7±31.3	< 0.05

Table 4 : Comparison of APG between AMI patients associated with hyperglycemia with and without heart failure .

APG (mg/dL)	Patients with heart failure n=9	Compensated patients n=7	P value
Meant ± S.D.	216.6 ± 30.3	155.7 ± 13.1	< 0.001

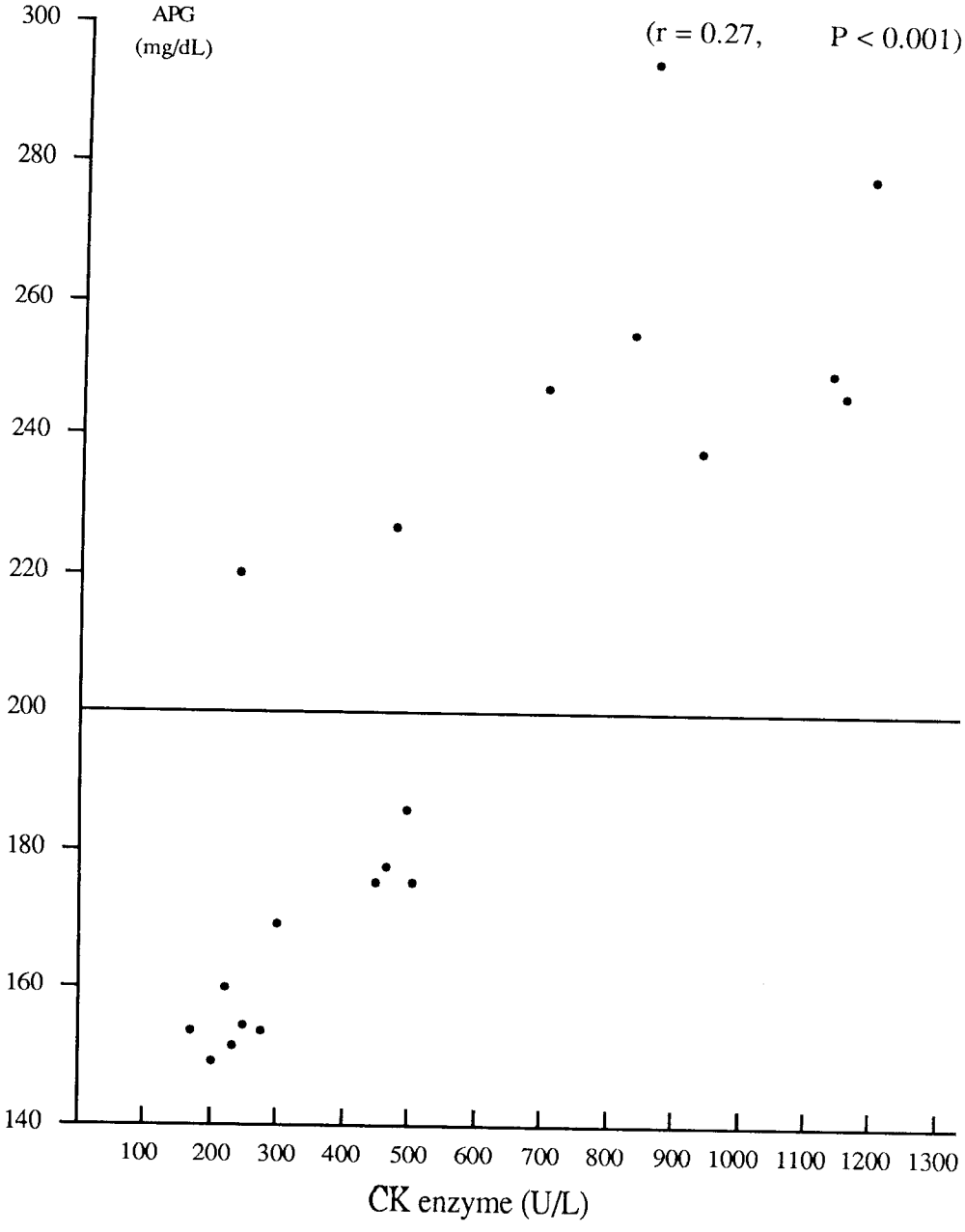

Figure 1: Relation of APG and CK enzyme in 20 patients with AMI and stress hyperglycemia .

DISCUSSION

Diabetics have a considerable excess mortality following AMI and tend to be at special risk of cardiogenic shock or refractory heart failure. On the other hand, the suggestion that diabetics with AMI are more likely to die from dysrhythmia has not been confirmed (Tansey et al., 1977).

Patients with undiagnosed diabetes and AMI might share the same risks and mortality.

The prevalence of undiagnosed diabetes in patients with AMI differs in several studies. Soler (1981) showed the prevalence of hyperglycemia in AMI patients, 9% as compared to the study of Oswald et al. (1984), 5.3% and the study of Madsen et al., (1986), 5.6%).

The higher prevalence of hyperglycemia reported by Lakhdar et al. (1984), 34% might be overestimate due to failure to eliminate the labile band of HbAlc and to empoly the WHO criteria for the diagnosis of hyperglycemia.

In the present study 18.6% of patients with AMI had hyperglycemia without previous history of diabetes. Soler (1981) originally suggested that determination of HbAlc could be used to distinguish between stress hyperglycemia and hyperglycemia due to undiagnosed diabetes. The present and previous studies (Madsen et al., 1986) suggest that determination of stable HbAlc is a valid method to separate stress from diabetes induced hyperglycemia and identifying those patients who may need treatment. However, in certain instances, such as chronic renal failure, isolated elevation of HbAlc level may be encountered when the plasma glucose level is normal (De Boer et al., 1980).

In the present study we used APG level of > 144 mg/dL and HbAlc level of > 8.5% as a combined diagnostic criteria of diabetes and indentified 5.3% of patients with AMI as previously undiagnosed diabetes and 13.3% had stress hyperglycemia as they had APG > 144 mg/dL with a normal range of HbA_{1c}.

They had a poor correlation between APG and HbAlc level, which is explained by stress induced hyperglycemia.

The mortality rate due to cardiogenic shock among this group of AMI with stress hyperglycemia was 20%. APG was significantly higher in non-survivors than in survi-

vors. Indeed all patients with APG above 220 mg/dL and normal HbAlc either died in hospital from their AMI or developed heart failure.

Our study pointed to a relation between hyperglycemia and heart failure and poorer prognosis.

Among the 16 survived patients with stress hyperglycemia 9 patients developed heart failure, such patients with heart failure had a higher APG than compensated patients.

Peak creatine kinase activity correlates well with more specific measures of infarct size, as well as with both long term and short term mortality after AMI (Thompson et al., 1979), and as such is a reasonable estimate of the extent of myocardial necrosis.

In this study, there was a correlation between enzymatically determined infarct size and APG concentration, which confirms that stress hyperglycemia is a real phenomenon in non diabetic patients with AMI, and that poor outcome in such patients predominatly reflects the clinical course of the extent of underlying infarction.

Several groups have attempted to define the cause of hyperglycemia after AMI. Some investigators have found cortisol, adrenaline and noradrenaline to be the main cause of hypercemia in AMI in non-diabetic patients (Oswald et al., 1986).

Catecholamine levels increase within the first 2 hr. after the onset of AMI (Karlseberg, 1981) and high concentrations of serum cortisol, growth hormone, and fatty acids are reached. These changes along with elevated glucagon values, persumbly contribute to glucose intolerance and peripheral insulin resistance (Bellodi et al., 1989). In experimental myocardial infarction it has been suggested that the stimulus to adrenaline release is a reflex arising from receptors at the site and boundary of infarct (Staszewska, 1971).

Catecholamines level are related to infarct size (Vaney et al., 1984). Therefore, it is not suprising that a correlation was found between APG and enzymatically determined infarct size.

On the other hand, insulin release from the pancreas is reduced in the early hours of AMI, the insulin response to tolbutamide infusion is nearly absent when AMI is complicated by cardiogenic shock and it gradually returns to normal with improvement of haemodynamics (Vetter, 1974).

In conclusion, hyperglycemia seen on admission in non-diabetic patients with AMI is an important prognostic indicator. The increased output of catecholamines and cortisol, and reduced insulin release, impair myocardial uptake of glucose (the main sourse of energy for ischemic myocardium), (Hansen et al., 1986). An inceased output of free fatty acids (which would be inhibited by insulin) may be associated with increased myocardial oxygen consumption and a predisposition to arrythmias (Liedke, 1981).

The experimental use of glucose insulin-potassium reduced infarct size (Balby, 1981).

Clark et al., (1985) showed that continuous intravenous infusion of insulin in diabetics with AMI had reduced mortality from 42% to 17%.

Studies of the effect of maintaining normoglycemia on the clinical course of hyperglycemic patients with AMI are necessary.

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نسبة وخطورة أرتفاع نسبة السكر فى الدم فى مرضى جلطة الشريان التاجى الحادة

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تم دراسة ١٥٠ مريضاً بجلطة الشريان التاجى الحادة ، ولقد وجد أن هناك ٥٠٣٪ فهم مصابين بمرض السكر الخفى ، و١٣.٣٪ مصابين بأرتفاع نسبة السكر فى الدم أرتفاعاً مؤقتاً ، وهذا الأرتفاع المؤقت لا يحتاج لعلاج حيث أن نسبة السكر قد عادت إلى المستوى الطبيعى بعد أيام قليله من حدوث جلطه الشريان التاجى . ولقد وجد أن هناك علاقة بين مستوى السكر فى الدم ومستوى أنزيم الكرياتين - كينز فى الدم الذى يقيس كمية الأحتشاء فى عضلة القلب ، أيضاً وجد أن مستوى السكر فى الدم أعلى فى مرضى جلطة الشريان التاجى مع هبوط بالقلب عنه فى المرضى ذو القلب المتكافئ .

مما سبق نستنتج أن زيادة نسبة السكر فى الدم فى مرضى جلطة الشريان التاجى الحادة ذو دلالة هامة فى حدوث مضاعفات لهؤلاء المرضى ، وأن أستخدام محلول الجلوكوز مع الأنسولين والبوتاسيوم فى هذه الحالات قد يفيد فى تقليل حجم أحتشاء القلب .