Carbohydrate Tolerance Status in Patients with Myocardial Infarction

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Hyperglycemia is an important independent risk factor in the development of coronary artery disease. Sixty one patients suffering from chronic and acute myocardial infarction out of which 12 patients were diabetic and 10 normal control subjects were investigated. The patients without diabetes and control subjects were subjected to oral and intravenous glucose tolerance tests. It was observed that the post load glucose level of most of the patients and fasting insulin level of patients without diabetes were higher as compared with control subjects. From the intravenous glucose tolerance test, half life of glucose and glucose assimilation coefficient were determined. Half life of glucose was increased significantly and glucose assimilation coefficient was decreased in the patients with myocardial infarction as compared with those of control subjects. The observations confirm that carbohydrate intolerance in myocardial infarction is not due to suppression of insulin secretion but due to peripheral utilization.

Introduction

Although abnormalities of both carbohydrate and lipid metabolisms were found to be associated with ischemic heart disease, comparatively little attention has been given to the study of carbohydrate metabolism. Hyperglycemia is an important risk factor in the development of coronary artery disease which is the major cause of death in diabetic patients. The high mortality was accounted for by the high prevalance of coronary disease in diabetic patients but also by its severity [1]. The presence of transient hyperglycemia and glycosuria in non-diabetic patients as a consequence of myocardial infarction and the occurrence of latent diabetes, which is often not recognized, perhaps because it is rarely looked for, have been reported [2]. A large number of patients with acute myocardial infarction showed carbohydrate intolerance which was related to the degree or arterial irregularity. Increased level of immunoreactive insulin in maturity onset diabetic patients has been reported from this laboratory [3] and insulin resistance exists in these patients with a decrease in number of insulin receptors on erythrocytes which indicates that insulin mediated glucose disposal is impaired [4]. Stress due to myocardial shock alongwith raising of glucose level by adrenaline secretion and glycogenolysis also cause increased secretion of cortisol or glucocorticoids which may be contributory towards persistent hyperglycemia seen in these cases [5]. The present investigation describes the carbohydrate tolerance status in patients with myocardial infarction.

Materials and Methods

Sixty one patients suffering from chronic and acute myocardial infarction admitted as indoor patients in National Institute of Cardiovascular Diseases, Karachi, were investigated, out of which 12 patients were diabetic. Only those patients were selected who had normal serum albumin, alkaline phosphatase and bilirubin. Patients receiving diuretic and oral hypoglycemic drugs were stopped for at least 48 h before the test. In diabetic group of patients only fasting and postprandial blood samples were drawn while other myocardial infarction patients were subjected to oral or intra-venous glucose tolerance test. The diagnosis of myocardial infarction was based on patients history and chest pain (intense) for a duration longer than 2 h and not relieved by nitroglycerine, electrocardiogram, elevated levels of alanine transferase and lactic dehydrogenase. The chronic myocardial infarction group comprised of those patients who had recovered from an earlier attack but were admitted with renewed symptoms and chest

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pain, dyspnea etc. Their electrocardiogram revealed a characteristic pattern of chronic infarction.

Ten normal healthy persons with a similar age group and socioeconomic status as that of patients were also studied as control subjects. They were medically examined and had no history of diabetes or cardiovascular disease. Their blood pressure and electrocardiogram were also normal. In the control group oral and intravenous glucose tolerance tests were done.

For oral glucose tolerance test, 0.5 gm of glucose per kg body weight was given orally to overnight (10–12 h) fasted individuals and blood samples were drawn at every 30 min interval for 2 h. For intravenous glucose tolerance test, fasting sample was drawn from the overnight (10–12 h) fasted subjects and 1 ml of a 50% glucose solution per kg body weight (0.5 gm glucose per kg) was injected intravenously within 90 sec. The first sample was collected at 5 min and called as zero time sample and other samples were collected at every 15 min of interval for 1 h followed by a single sample at 2 h. The results of blood sugar determination of intravenous glucose tolerance test were plotted on a semilogarithmic graph to determine the half life of administered glucose in the blood and glucose assimilation coefficient was calculated by the following formula:

$$C_{(t)} = C_{(o)}\, e^{-kt}$$

where $C_{(t)}$ is glucose in mg/dl at any particular time (t), $C_{(o)}$ is the glucose in mg/dl immediately after infusion and K is the assimilation constant. In case $C_{(t)} = 1/2\ C_{(o)}$, t is half life period of glucose. K is expressed as percent per minute at a point of time of half life period. K in normal metabolic state is between 1.4 to 2.0 and when K is more than 2, it indicates increased glucose tolerance, when K is less than 1.1 it indicates diabetic metabolic state and between 1.1 and 1.25, it is suspected diabetic metabolic state [6].

Blood glucose was estimated by Nelson-Somogyi method [7], blood lactic acid by Barker and Summerson method [8], blood pyruvate by Friedman and Haugan method [8], total cholesterol by Ferro and Ham method [9], serum triglyceride by the method of Fletcher by Sigma kit supplied by Sigma Chemical Co., St. Louis, U.S.A., inorganic phosphorus by Fiske and Subbarow method [7], sodium and potassium by flame photometry and immunoreactive insulin by radioimmunoassay kit (supplied by Radiochemical Centre, Amersham, Buckinghamshire, England).

Table I. Physical features and different blood analytes in control subjects and myocardial infarction patients with or without diabetes. The values are mean ± s.e.m. The number of observations or units is given in parentheses.

	Control subjects	Myocardial infarction patients without diabetes	Myocardial infarction patients with diabetes
Age (years)	48.8 ± 2.1 (10)	53.9 ± 2.1 (49)	51.6 ± 3.3 (12)
Sex male	6	47	12
female	4	2	–
Body weight (kg)	57.6 ± 1.7 (10)	62.5 ± 1.3* (49)	61.5 ± 1.5 (12)
Blood pressure systolic	122.0 ± 1.0	123.1 ± 3.1	137.3 ± 6.3
(mm Hg) diastolic	78.7 ± 2.1 (10)	86.2 ± 2.9 (49)	87.1 ± 3.5 (12)
Smokers (%)	50.0	81.6	75.0
Pulse (per min)	73.8 ± 1.0 (10)	86.8 ± 2.7 (49)	94.3 ± 5.7 (12)
Duration of cardiac illness (months)	–	24.6 ± 5.1 (49)	31.8 ± 7.7 (12)
Duration of diabetes (months)	–	–	41.4 ± 6.7 (12)
Family history (%)			
for diabetes	–	4.1	8.3
for hypertension	–	24.4	8.3
for hypertension and diabetes	–	32.7	66.7

Table I. Continued.

	Control subjects	Myocardial infarction patients without diabetes	Myocardial infarction patients with diabetes
Serum analytes			
Lactate (mmol/l)	0.9 ± 0.06 (10)	1.7 ± 0.06* (49)	1.8 ± 0.1* (12)
Pyruvate (mmol/l)	0.09 ± 0.01 (10)	0.15 ± 0.01* (49)	0.16 ± 0.02* (12)
Cholesterol (mg/l)	1491.0 ± 36.2 (10)	2301.5 ± 50.2* (49)	2625.0 ± 46.8* (12)
Triglyceride (mg/dl)	91.4 ± 1.7 (10)	171.2 ± 1.9* (49)	178.7 ± 5.2* (12)
Inorganic phosphate (mg/dl)	3.8 ± 0.3 (10)	3.6 ± 0.1 (49)	3.4 ± 0.2 (12)
Sodium (meq/l)	129.8 ± 2.5 (10)	136.4 ± 1.1 (49)	134.2 ± 1.8 (12)
Potassium (meq/l)	4.2 ± 0.2 (10)	4.4 ± 0.1 (49)	4.3 ± 0.3 (12)
Oral glucose tolerance test			
Fasting (mmol/l)	4.7 ± 0.1	5.6 ± 0.1*	8.2 ± 0.3*
30 min (mmol/l)	6.9 ± 0.5	7.3 ± 0.2*	–
60 min (mmol/l)	4.4 ± 0.3	9.0 ± 0.2*	–
90 min (mmol/l)	–	7.4 ± 0.2*	–
120 min (mmol/l)	4.0 ± 0.2 (10)	5.7 ± 0.1* (26)	–
Postprandial (mmol/l)	–	–	17.1 ± 0.6* (12)
Intravenous glucose tolerance test			
Fasting (mmol/l)	4.7 ± 0.1	6.1 ± 0.2*	–
5 min (mmol/l) (zero time)	9.4 ± 0.7	12.2 ± 0.5*	–
15 min (mmol/l)	8.2 ± 0.6	10.9 ± 0.6*	–
30 min (mmol/l)	6.9 ± 0.5	9.1 ± 0.4*	–
45 min (mmol/l)	5.1 ± 0.4	7.5 ± 0.4*	–
60 min (mmol/l)	4.4 ± 0.3	6.3 ± 0.3*	–
120 min (mmol/l)	4.0 ± 0.2 (10)	5.3 ± 0.2* (23)	–
Half-life of glucose (min)	52.3 ± 1.5 (10)	66.3 ± 4.7* (23)	–
Glucose assimilation coefficient	1.4 ± 0.03 (10)	1.1 ± 0.04* (23)	–
Serum immunoreactive insulin			
Fasting (μU/ml)	13.4 ± 3.3	27.7 ± 4.6*	15.6 ± 3.4
30 min (μU/ml)	50.6 ± 8.7	81.9 ± 16.0	–
60 min (μU/ml)	32.4 ± 4.4	47.9 ± 10.8	–
Postprandial (μU/ml)	– (5)	– (8)	40.3 ± 5.1** (4)

* $P < 0.05$ as compared with control subjects.
** $P < 0.05$ as compared with fasting values.

Results and Discussion

The established risk factors for ischemic heart disease are hypercholesterolemia, hypertension, smoking, diabetes mellitus, age and sex [10]. The mean body weight of the myocardial infarction patients without diabetes was higher than the control group while the age, blood pressure and pulse rate were not different and majority of the subjects was male. Serum lactate and pyruvate levels were significantly higher in myocardial infarction patients without diabetes as compared with control group but when the values were compared between myocardial infarction patients with or without diabetes, then so significant difference was observed (Table I). The

stress factor in such conditions could be responsible in raising the pyruvate and lactate levels while lactic acidosis is usually present in diabetic patients.

In the present study it was observed that serum cholesterol and triglyceride increased in patients of myocardial infarction and there was no difference in triglyceride level in patients with or without diabetes. The patients with coronary artery disease show hypercholesterolemia or hypertriglyceridemia which have been used as a prognostic indicator of atherosclerotic complication. The decrease in inorganic phosphate and potassium has been implicated with diminished carbohydrate tolerance but these parameters were not found decreased in patients with myocardial infarction patients with or without diabetes. Diabetes mellitus is among the major risk factors associated with ischemic heart disease. Insulin may increase cholesterol synthesis by stimulation of the rate limiting enzyme hydroxy-methyl-glutaryl-CoA reductase. This mechanism could operate to produce hypercholesterolemia when either endogenous or exogenous hyperinsulinemia is present [11]. Oral glucose tolerance test was done on myocardial infarction patients without diabetes which showed decreased tolerance and exhibited a diabetic type of curve. The fasting blood sugar as well as the other values up to 2 h were significantly higher in most of the patients as compared with control subjects. It has been suggested that hyperglycemia is an independent risk factor in coronary artery disease and is as important as hypercholesterolemia. Most of the patients with myocardial infarction also had higher fasting immunoreactive insulin as compared with control subjects. The precise cause of increased insulin secretion in myocardial infarction patients is not known but it may cause lipid accumulation in the arterial wall as it does in adipose tissue.

In myocardial infarction patients with diabetes only postprandial glucose level was determined and the values showed that of typical diabetic patients. High postprandial level of immunoreactive insulin in diabetic patients with myocardial infarction along with impaired glucose tolerance indicate some insulin antagonism. The excessive insulin secretion in patients with coronary heart disease secondary to glucose intolerance probably induces hepatic synthesis of triglyceride which is a characteristic of potential diabetics.

Intravenous glucose tolerance test permits the calculation of glucose utilization coefficient from the relationship of blood glucose and time. In the present study the value of blood glucose at different time intervals in patients with myocardial infarction were significantly higher than those of normal control subjects. The half-life of glucose in blood of patients with myocardial infarction was significantly longer and the glucose assimilation coefficient was significantly lower than those of the control subjects (Table I). The longer half-life of glucose and lower assimilation coefficient of glucose in patients suggest impairment of carbohydrate tolerance. Therefore it is reasonable to suggest that many patients with cardiac infarction are potential diabetics although they show mild carbohydrate intolerance. Whether the abnormalities in carbohydrate tolerance and in plasma insulin level are different stages of the same basic disorder or it is a syndrome with multifactoral etiology is not known.

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