

A PROSPECTIVE FOLLOW UP STUDY OF PATIENTS WITH NEWLY DIAGNOSE MATURITY ONSET DIABETES MELLITUS

Pages with reference to book, From 35 To 38

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Abstract

In a prospective study of 332 patients with newly diagnosed maturity onset diabetes mellitus, the frequency of complications was monitored over a period ranging from 3 to over 7 years. The groups included 97 patients on diet, 209 on oral hypogly-caemic agents and 26 on insulin. Approximately 10% of the patients showed evidence of early retinopathy at the time of diagnosis.

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On follow up the frequency of myocardial ischaemia was relatively higher in the group taking oral drugs, which also was the largest group and had a relative excess of adverse factors at the time of diagnosis. The overall frequency of microvascular diseases as evidenced by retinopathy was similar in all the groups on follow up. When the emergence of complication was analysed in relation to control of blood glucose, the degree of control did not affect the relative frequency of myocardial ischaemia within the individual treatment groups. However, the control of diabetes exerted a favourable influence on the frequency of microvascular diseases in the groups taking dietary treatment or insulin (JPMA 31:35, 1981).

Introduction

Diabetes mellitus is characterised by hyper-glycaemia and progressive Vascular disease leading to increased morbidity and mortality. With the discovery of insulin and oral hypogly-caemic agents, it was hoped that both the short term and the long term complications would be controlled effectively. The exact relationship of blood sugar control and risk of complications is not clear. The findings of University Group Diabetic Programme (UGDP, 1970) showed that the frequency of vascular complications increased following the use of oral hypoglycaemic agents. The observation is important in the management of diabetes. The spectrum of diabetes in Pakistan is presently being studied and initial observations have been recorded (Haider and Obaidullah, 1980). The purpose of this study was to do a long term prospective follow up of patients with newly diagnosed diabetes mellitus with a view to monitor the emergence of complications in relation to the degree of control and the type of treatment.

Material and Methods

The patients selected were newly diagnosed untreated diabetics who had symptoms of the disease for less than a year. The study was started in 1972 and till 1977, 584 patients were studied. The present analysis deals only with 332 patients who have completed a satisfactory follow-up of at least 3 years till January, 1980. Each patient had a baseline assessment and investigations (Haider et al., 1978). Each patient underwent a complete yearly physical examination and laboratory investigations and during the follow-up period any new complications were recorded.

The changes were observed in blood pressure, fundus examination, ECG heart size, peripheral pulses, kidney function and neurological examination and the following points were recorded:-

1. Death

2. Cardiovascular events.

- (a) ECG changes of ischaemia: new changes.
- (b) Myocardial infarction: as a new event or worsening of the previous clinical condition.
- (c) C.V.A. (cerebrovascular accidents).
- (d) Peripheral vascular disease.

3. Microvascular disease.

- (a) Retinopathy: new changes or worsening of the grade.
- (b) Albuminuria: more than a trace, without any other cause such as infection.

4. Neuropathy

All patients on recruitment were instructed to control their diabetes by dietary discipline and the response was assessed after 4-6 weeks. Those not controlled on diet were given the choice of either sulphonylureas or insulin. Ninety seven patients continued on diet, 209 were treated with sulphonylurea and 26 were given insulin injection. Those patients in whom dietary therapy failed at any stage during follow up and were changed to sulphonylurea/or insulin were counted in the treatment group at the time of assessment. All biochemical examinations were made by method described by King and Wooten (1964). The ECG's were interpreted according to the Minnesota Code (Blackburn, 1969). The cholesterol estimations were done by the method of Abell et al (1952).

Results

Table I: Age and Sex Distribution of 332 Patients with Newly Diagnosed Diabetes Mellitus in Various Treatment Groups

<i>Age (Years)</i>	<i>Diet (97)</i>		<i>Oral anti-diabetic (209)</i>		<i>Insulin (26)</i>	
	<i>Male</i>	<i>Female</i>	<i>Male</i>	<i>Female</i>	<i>Male</i>	<i>Female</i>
<30	1	2	4	8	3	1
31-40	13	21	19	38	5	8
41-50	12	23	27	54	3	2
51-60	11	13	13	40	1	3
61 and above	—	1	4	2	—	—
Total	37	60	67	142	12	14

Table I shows the distribution of patients according to age and sex in various treatment groups. There were 97 patients (37 males and 60 females) on diet, 209 (67 males and 142 females) on oral anti-diabetics and 26 (12 males and 14 females) were on insulin therapy. Most of the patients in each group were between the ages 31-50 years.

Table II: Distribution of Patients According to the Clinical and Laboratory Findings at the Time of Diagnosis in the 3 Treatment Groups

<i>Clinical Findings</i>	<i>Diet (97)</i>	<i>Oral anti-diabetic (209)</i>	<i>Insulin (26)</i>
Blood sugar postparandial > 250 mg%	40 (41.2 %)	120 (57.6 %)	14 (53.84%)
Blood cholesterol > 250 mg%	9 (9.27%)	34 (16.3 %)	1 (3.85%)
Obesity > 10 of standard wt.	13 (13.39%)	54 (25.9 %)	1 (3.85%)
Hypertension	13 (13.39%)	31 (14.88%)	1 (3.85%)
H/O. Angina	5 (5.15%)	8 (3.84%)	2 (7.7 %)
ECG (ischemic changes)	7 (7.19%)	33 (15.84%)	—
Peripheral circulatory abnormality	—	—	—
Retinopathy	9 (9.27%)	23 (11.04%)	3 (11.54%)
Protein uria	7 (7.19%)	20 (9.6 %)	2 (7.7 %)

Table II shows the clinical and laboratory finding at the time of diagnosis. In the group of patients taking oral drugs there was a slightly higher frequency of those with a post-parandial blood sugar of 200 mg%, cholesterol 250 mg%, obesity (> 10% of the standard weight) and ECG abnormalities. Approximately 10% of the patients had evidence of microvascular changes at the time of assessment.

Table III: Distribution of Patients According to New Complications During Follow Up in the 3 Treatment Groups

<i>Complications</i>	<i>Oral anti-diabetic (209)</i>		
	<i>Diet (97)</i>	<i>Oral anti-diabetic (209)</i>	<i>Insulin (26)</i>
Myocardial ischaemia	7 (7.21%)	30 (14.4 %)	1 (3.85%)
Hypertension	15 (15.45%)	26 (12.48%)	1 (3.85%)
Cerebrovascular accident	—	1 (0.45%)	—
Retinopathy	9 (9.27%)	19 (9.31%)	3 (11.54%)
Protein uria	6 (6.18%)	10 (4.8 %)	1 (3.85%)
Neuropathy	—	3 (1.44%)	—
Deaths	—	4 (1.92%)	—

Table III shows the frequency of new-events during the period of follow up in patients taking various forms of treatment. There was a relatively higher frequency of clinical evidence of myocardial disease or ischaemic changes in ECG in patients taking oral drugs. The frequency of micro-vascular diseases was approximately similar in all groups.

Objective signs of neuropathy were seen in 3 patients taking the oral drugs. Four patients on sulphonylureas died of cardiac failure.

Table IV: Relationship of Blood Sugar Control on New Complications in the 3 Treatment Groups

<i>Complications</i>	<i>Diet (97)</i>		<i>Oral anti-diabetics (209)</i>		<i>Insulin Inj. (26)</i>	
	<i>Good (77)</i>	<i>Poor (20)</i>	<i>Good (95)</i>	<i>Poor (114)</i>	<i>Good (17)</i>	<i>Poor (9)</i>
Deaths	—	—	—	4(3. 5%)	—	—
Myocardial ischaemia	6 (7.78%)	1 (5%)	12 (12.63%)	18 (15.80%)	1 (5.9%)	—
Cerebrovascular accidents	—	—	1 (1.05%)	—	—	—
Retinopathy	4 (5.20%)	5 (25%)	8 (8.40%)	11 (9.65%)	1 (5.9%)	2 (22.22%)
Nephropathy	2 (2.60%)	4 (20%)	3 (3.5%)	7 (6.1 %)	—	1 (11.11%)
Neuropathy	—	—	—	3 (2.60%)	—	—

Table IV shows the relation of blood sugar control with complications. The diabetic control was assessed on the basis of the mean of the last 3 readings of the post-parandial blood sugar. The mean of the blood glucose level <200 mg% was considered as satisfactory control.

Of 97 patients on diet, myocardial ischaemia was recorded in 6 out of 77 patients (7.78%) with

satisfactory control and one out of 20 patients (5%) with poor control. Amongst patients on oral drugs, ischaemic changes were detected in 12 out of 95 well controlled patients (12.63%) and 18 out of 114 poorly controlled patients (15.80%) on oral hypoglycaemic drugs. In the insulin group, one out of 17 patients (5.90%) with good control showed ischaemic changes.

There was a relatively higher frequency of retinopathy in those who were poorly controlled either on diet or insulin. In the group taking oral drugs the frequency of further progress in diabetic retinopathy was equally distributed in the good and poorly controlled groups. Three cases of neuropathy occurred in poorly controlled patients taking sulphonylureas. There were 4 deaths which also occurred amongst poorly controlled subjects on oral drugs.

Table V: Duration of Follow Up of 332 Patients.

<i>Duration (years)</i>	<i>Patients</i>	<i>Percentage</i>
3 to 5	145	43.64
> 5 to 7	151	45.4
> 7	36	10.89

Table V shows duration of follow up in 332 patients; 154 cases (43.64%) were followed up for 3 to 5 years, 151 patients (45.4%) from over 5 years to 7 years and 36 patients (10.89%) were followed up for more than 7 years.

Discussion

Despite the availability of insulin and oral hypoglycaemic agents to control hyperglycaemia in diabetes mellitus, the chronic vascular complications continue to occur.

The value of the rigid control of blood glucose in reducing the frequency of various complications still remains controversial. The views of those who support the maintenance of rigid control of blood sugar has been forcefully expressed in a policy statement of the American Diabetic Association. Cahill et al (1976) believe that there is sufficient clinical and experimental data to demonstrate the benefit of maintaining rigid control of blood glucose. Siperstein et al (1977) have expressed doubts about the association between microvascular complications and degree of hyperglycaemia. They have cautioned against the over zealous use of insulin to the point of producing hypoglycaemic episodes. Their views have also been supported by others (Knowles, 1964; Bondy and Felig, 1971). The data of University Group Diabetic Programme (Goldner et al., 1971) failed to show any effect of lowering blood sugar. This prospective follow up study of newly diagnosed diabetics has been done under considerable limitations. The randomisation of patients to various treatment groups was done on the basis of clinical necessity. The patient's compliance to prescribed treatment and assessment was done indirectly by cross-questioning and the number of patients in various groups was not balanced.

Myocardial ischaemia developed more frequently in those on oral hypoglycaemic agents but the clinical findings suggestive of this complication were present in this group at the time of diagnosis.

Microvascular disease in the form of retinopathy was present in nearly 10% of diabetics at the time of diagnosis and its frequency during follow up remained the same in all treatment groups. A few cases of cerebrovascular accidents, neuropathy and deaths occurred in patients on oral therapy. The relative

frequency of myocardial ischaemia was unaffected by the level of control of blood sugar in all the three treatment groups. The frequency of retinopathy was much higher in poorly controlled and lower in well controlled patients on diet and insulin treatment. The retinopathy in patients taking tablets was unaffected by the degree of blood glucose control. The study in spite of its limitations cautions against the indiscriminate use of oral hypoglycaemic agents. Diet control and insulin therapy seem to reduce the frequency of microvascular complications. Reduction of impact factors like hypertension, smoking and hyperlipidaemias along with a good control of blood sugar are likely to minimize the risk of ischaemic heart disease in diabetics.

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