Transition of Type 2 Diabetes Patients From Oral Hypoglycemic Agents to Insulin Therapy

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Abstract

Background: The treatment options for type 2 diabetes have expanded rapidly in recent years with the development of new oral therapies, the abilities of these agents to lower blood glucose to reach and sustain glycemic targets in some patients is limited. Insulin has been wrongly viewed traditionally as a last resort to be used only when all other treatment options have been exhausted; however significant improvements in insulin therapy are beginning to remove the barriers to initiation of insulin replacement in type 2 diabetes.

Objectives: To screen the criteria of type 2 diabetes patients who were treated with insulin in this sample study, and the effect of transition to insulin on glycemic parameters, in comparison to their follow patients who are still on oral hypoglycemic drugs

Patients and Methods: Across-sectional design and a convenient sampling procedure were adopted to enroll 200 patients who met the inclusion criteria and were attending the National Diabetes Center for Treatment and Research in Al-Mustansiriya University during the period from 1st of February 2009 to the end of March 2009, each patient included in study sample were interviewed directly by similar questionnaire, same measurement and investigation were applied to all patients.

Results: The means of age of onset and duration of diabetes mellitus for patients on insulin and patients on oral hypoglycemic agents therapy were (44.56±9.03)(48.91±9.45)(12.64±7.2)(6.91±6.38) years respectively, there was a statistically significant difference among means of the two groups, while there was no significant difference between means of all other criteria and glycemic indicator of both group.

Conclusion: Apart from the means of age of onset and the duration of diabetes which shows significant difference between the two groups of patient in this study (those on Insulin therapy versus those on oral hypoglycemic agents and oral diet therapy), all other means of variable used in this study show no significant difference between the two groups of patients.

Key words: Insulin – Type 2 diabetes mellitus.

Introduction:

There are two defects that together cause type2 diabetes, impaired insulin secretion with progression towards insulin deficiency and insulin resistance, impaired insulin secretion is a result of initial beta cell dysfunction and subsequent insulin deficiency, while insulin resistance results in increased hepatic glucose production and reduced peripheral glucose uptake[1].

There is evidence that beta cell dysfunction begins prior to the onset of type2 diabetes and indeed , can predict the progression from normal glucose tolerance to impaired glucose tolerance to type 2 diabetes [2].

The United Kingdom Prospective Diabetes Study (UKPDS) demonstrated an inexorable decline in beta cell function and therefore, insulin secretion over time in patients with type2 diabetes, despite oral therapy, indicating a clear need for insulin therapy in these patients if blood glucose control targets are to be met and maintained [3]. Short term intensive therapy has been shown to improve insulin resistance, possibly by correcting glucotoxicity and lipotoxicity [4]. Furthermore, the reduced strain on the beta cell by insulin therapy can potentially induces beta cell rest which results in increased insulin secretion [5].

One could speculate from these observations that earlier initiation of insulin therapy perhaps even from disease onset could preserve beta cell function and thus insulin secretion which could prevent disease progression and improve glycemic responses to supplemental oral treatment if needed [4].

Insulin resistance is a major pathogenic defect in type 2 diabetes and correlations with obesity and hyperinsulinemia have resulted in misconception of the role of exogenous insulin therapy [6]. So that despite concerns that insulin treatment may, therefore, worsen insulin resistance where as many studies have demonstrated that short term intensive insulin therapy actually improves insulin resistance[7].

Furthermore, the (UKPDS) provided no evidence of an increased incidence of atherosclerotic events in people with type 2 diabetes who were treated with insulin versus those who did not receive insulin [8].

Patients and Methods:

Collection of data was carried out during the period between 1/2/2009 and 30/3/2009. Two – hundred type 2 diabetic patients were enrolled in this study from those who were attending to the National Center for the Treatment and Research of Diabetes in Al-Mustansiriya University, systematic random sampling technique was used for selection of the sample, daily selection of the first patient was done randomly, subsequently patients were selected every other one. All type 1 diabetic patient treated with insulin at time of diagnosis of diabetes mellitus excluded from the study, each patient in the study group was interviewed directly and asked to answer the following questions (age, sex, age of onset of diabetes mellitus, type of treatment at time of diagnosis with diabetes mellitus, duration of diabetes mellitus , type of treatment at time of study ,as for patients treated with insulin they were asked about

the time of transition from oral hypoglycemic agent to insulin). Then after weight, height, body mass index and waist hip ratio, systolic and diastolic blood pressures were measured for each patient in the study sample during interview. The following laboratory investigation and tests were done for each patient (FPG-glycated hemoglobin HbA1c – serum cholesterol – serum triglyceride).

Results:

The mean age ± SD for the study sample was (56.15 ± 9.93) years and the proportions of males and females were (48%, 52%) respectively, therefore the means ± SD for age of onset and duration of diabetes for (200) patients included in this study were (47.63± 9.52) (8.6 ± 7.1) years respectively. all patients were treated by diet and oral hypoglycemic agent at time of diagnoses of diabetes and the percentage of patients who were treated by insulin at time of study were 59 patients (29.5%) .Table (1) The minimum, maximum, means ± SD of time which is spend by the patients since the time of diagnosis until the shifting to insulin therapy were (1, 24, 9.92± 6.83) years respectively.

There was no significant difference between means of the following variables for patients treated with insulin and patients still managed by diet±oral hypoglycemic agent (age, body mass index, waist hip ratio, systolic and diastolic blood pressure, fasting blood glucose, glycated hemoglobin, total serum cholesterol, and serum triglyceride). No significant distribution was found among males and female patients and type of treatment at the time of the study. Whereas significant difference was found between means of age of onset of diabetes for patients treated with insulin and patients treated with diet and oral hypoglycemic agents, it was (44.56±9.03) (48.91±9.45) years respectively (p=0.03), also there was a significant difference was found between means of duration of diabetes for patients treated with insulin and patients treated with diet and oral hypoglycemic agents, it was (12.64±7.2) (6.91±6.38) years respectively**,** (p<0.00001). Table (2**)**

Table (1): Patients criteria (age, sex, age of onset, duration of diabetes, type of treatment, time of transition to insulin)

Patients criteria		Means±SD
Age		56.15 ± 9.93 Years
Age of onset		47.63±9.52 Years
Duration of DM		8.60±7.4 Years
Time of transition		9.92±6.83 Years
Sex	**Male**	48%
	Female	52%
Type of treatment	**Oral ± diet**	70.5%
	Insulin	29.5%

Table (2): Distribution of variables among patients treated with insulin or oral hypoglycemic agents

Variable	Insulin therapy		Oral therapy		
	59		**141**		
	Mean ± SD		**Mean ± SD**		**t-test:d.f:p**
Age	57.14 ± 10.23		55.74±9.81		0.907:198:0.36
Age of onset of DM	44.56±9.03		48.91±9.45		3.01:198:0.03
Duration of DM	12.64±7.2		6.91±6.38		5.57:198:0.00001
Body mass index	29.31±5.20		29.54±4.96		0.291:198:0.77
Waist hip ratio	0.95±0.06		0.96±0.06		1.11:198:0.26
SBP	144.66±23.59		142.91±19.80		0.539:198:0.59
DBP	87.03±10.83		89.22±10.74		1.3:198:0.19
FBG	188±23		179±19		0.817:198:0.41
HbA1c	9.22±2.03		8.77±2.1		1.45:198:0.14
Total cholesterol	207.12±39.90		204.65±37.80		0.415:198:0.67
S. Triglyceride	141.41±57.64		149.45±69.08		0.787:198:0.43
Sex	No: 59	%	No:141	%	X^2: d.f:p
Male	23	31.8	72	51	1.7:1:0.18
Female	36	69.2	69	49	

t= t-test d.f= degree of freedom p= p value

Discussion:

The emerging epidemic of type 2 diabetes, coupled with finite health resources, requires the treatment of hyperglycemia to be simple and efficiently managed. Type 2 diabetes is a progressive disease and eventually almost all patients will require insulin to maintain good glycemic control. Knowing when and how to start insulin in general practice is central to the optimal management of type 2 diabetes. A more common problem is when and how to commence insulin in patients with type 2 diabetes that is in 'secondary

failure'. The term secondary failure refers to the 'failure' of oral hypoglycemic drugs to maintain glycemic control. The United Kingdom Prospective Diabetes Study (UKPDS), clearly showed that most people with type 2 diabetes will experience progressive pancreatic β cell dysfunction, despite excellent control. The secondary failure rate in this study was 44% after six years of diabetes. Since the time of the UKPDS, targets for glycemic control have become increasingly stringent so secondary failure of oral hypoglycemic drugs now occurs much sooner and is almost invariable[(3)].. The inevitable need for insulin therapy in most patients is best discussed early in treatment when the need for insulin therapy is not imminent. This message should be continuously reinforced as it helps to set expectations and eases the transition to insulin later on. In this study 200 patients were covered in an attempt to screen the criteria of patients who were treated with insulin therapy in type 2 Iraqi diabetic patients and the effect of insulin on the glycemic control of those patients, in comparison to their follow patients who are still on oral hypoglycemic drugs. A part from the age of onset and the duration of diabetes all other variable mention above were insignificance especially when it comes to glycemic control.59 patients were on insulin therapy which represents 29.5% of the total No. of the patients, none of them was having significant glycemic control difference from the patients who are still on oral hypoglycemic and diet therapy, and there was no significant different in the criteria that led to insulin therapy between the two groups .

Yet this study shows that the earlier the age of onset of the DM the more likely to start insulin, and the longer the duration of DM the more chance that the patients need insulin therapy, Which usually goes with the natural history of the disease as the longer the time the patients have diabetes the more the chances that insulin natural reserve in the beta cells will be depleted. The fact that all the variable that was mentioned above among both groups of type 2 diabetes (those on insulin and those on oral hypoglycemic agent) were of no significant value might indicate the need for reconsideration of how and when we start insulin therapy in type 2 Iraqi diabetic patients especially when it comes to achieving glycemic control, this study show that there are no significant difference in the glycemic control in both groups (fasting blood glucose. and glycated HbA1c). Many factors might attributed to those results and can be categorized to patients compliance and education or the doctors policy in treating patients and the fact that insulin is not available as it should be to make it easer for the patient to use it in a proper way and last but not the least the absence of proper follow up by the patients them self at home through the presence of self monitoring glucometers which is lacking for most of our patients. many patients refused insulin therapy for many reasons of which is the myth that their diabetes is worse if they are on insulin others found it easer for them to be on oral treatment though they are informed to take insulin by their doctors, some found it cheaper to be on oral hypoglycemic agent rather than insulin especially when the new costly types of insulin were introduced to the markets ,so patient compliance and education is a corner stone in initiating insulin therapy and this massage should be taken in consideration by all doctors that treat diabetic patients .yet some times it's the doctors who need to remove the barrier of starting insulin for the patients by knowing the facts that insulin is really needed it if they want to keep their patient within reasonable glycemic control .one of the major needs here is the presence or the availability of HbA1c in the Iraqi laboratories and the use of this marker as key marker in the follow up of the patients which is really not the true story for it neither available in the laboratories nor it is used by doctors in the way it should be.

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