Initiation of Basal Insulin in Patients with Uncontrolled Type 2 Diabetes Mellitus

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Abstract

Type 2 diabetes mellitus is a growing health problem, characterized by insulin resistance progressing to beta cell dysfunction and insulin deficiency, most of these patients will need intensification of treatment and initiation of insulin to delay or prevent diabetic complications. Glycemic control is the most important aspect in management, and in reducing morbidity and mortality of the diseases. Control of plasma glucose in patients with diabetes can be assessed by HbA1c, FPG, PPG, but still HbA1c% remains the gold standard for assessment of glycemic control and follow up of diabetic patients. The aim of this study is to assess HbA1c% in patients on oral anti-diabetic drugs, with poorly glycemic control before and after adding basal insulin, with titration of the dose of insulin depending of fasting blood sugar. 82 patients with uncontrolled type 2 diabetes (43.9% male, 56.1% female), with HbA1c more than 9%, on two types of oral diabetic medication or more, were started on basal insulin (glargine, lantus) and followed for three to six months. Overall 82 patients with type2 diabetes mellitus were included in the study. The mean age of the study population was 58.4 years, the mean duration of the disease range was 13.4 years. All patients with HbA1C more than 9%, without organ failure, were included in the study. The mean HbA1c overall had decreased from mean of 11.15% before starting basal insulin to the mean of 8.43% within 3 to 6 month , after initiating basal insulin , this difference was significant at p < 0.000 .There was no adverse effect to this medication in any of the study group. The addition of basal insulin to oral anti- diabetic medication in uncontrolled insulin-naïve type 2 diabetic patients resulted in significant improvement of glycemic control, with improved HbA1c level, without adverse effects.

Keywords

HbA1c-Haemoglobin A1c% , FBG-fasting blood glucose , PPG-post prandial glucose

INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a growing health problem, leading to morbidity and mortality. T2DM is characterized by insulin resistance progressing to beta cell dysfunction and insulin deficiency. T2DM accounts for 90% of all cases of diabetes, the vast majority of patients who are on oral hypoglycemic agents are uncontrolled, with above needed target of HbA1c level, and the glycemic

control tends to be worsen over time, these patients need insulin, as their ability to produce their own insulin from pancreatic beta cells declines progressively (Sanlioglu et al., 2013)

The UK Prospective Diabetes Study (UKPDS) highlighted the progressive nature of T2DM and the need for intensification of treatment, and initiation of insulin to maintain satisfactory glycemic control (UKPDS study 16)

Glycemic control in diabetes mellitus is needed to reduce morbidity and mortality of the disease. Achieving good glycemic control or significantly prevent or delay the micro vascular and macro vascular complications of diabetes. Glycated hemoglobin (HbA1c) is the gold standard for assessment of glycemic control (Ezra Belay et al., 2015)

This is a prospective study for uncontrolled insulin-naïve patients with type 2 diabetes mellitus on oral hypoglycemic drugs. all patients were on metformin plus sulfonylurea (glimepiride or gliclazide) started on basal insulin (glargine -lantus), in addition to their own oral anti- diabetic drugs and followed for three to six months to see the effect on glycemic control , by assessing HbA1c before and after starting the basal insulin.

METHODS

This was prospective study conducted from January to June 2018, for 82 patients following in my private and hospital clinic, 36 (43.9%) were male patients, and 46 (56.1%) were female. All these patients were on two or more oral anti- diabetic drugs including metformin, with suboptimal glycemic control, HbA1c% for all was above 9%, which indicate poor glycemic control, and need to initiate basal insulin (Allison Petznick et al., 2011)

The patients were documented and started on basal insulin, 10 units of glargine insulin (lantus) nocturnal dose, titration of the dose of insulin was through checking fasting blood glucose for three days, and taking the medium of the readings, following the guideline of (Basal Insulin Titration Algorithms From World Medical Societies) (table 1), or by checking fasting blood sugar once per week, by either calling by phone or attending the clinic weekly to adjust the doe of insulin.

RESULTS

Overall 82 patients with type 2 diabetes mellitus were included in the study 36 (43.9%) were male, and 46 (56.1%) were female. The mean age of the study population was 57.7 years, and duration of the disease range from 6 to 20 years with the mean of (13.2).

All patients with HbA1C more than 9%, without organ failure, who agreed to start insulin, were included in the study. The mean HbA1c overall had decreased from 11.15% to 8.44% at 3 to 6 month follow-up, this difference was significant at $p < 0.000$.

Reduction of HbA1c was not related to either patient age, duration of diabetes, the level of HbA1c % or the daily dose of basal insulin. The minimum dose of insulin was 10 units per day ,and maximum of 25 units, (mean of 16.6 units) ,the dose of insulin were titrated by checking the fasting blood glucose, none of patients in the study group gave any symptoms of hypoglycemia.

Measure algorithm	ADA/EASD40	ACCE/ACE41	IDF43	CDA44
Initial dosage	10U/d	10U/d	Non specified	10U/d
Titration	2U every 3 d	1-3 U every 2-3 d	2U every 3 d	1 U every d
Target FBG mg/ dl	70-130	<110	<110	72-126
Target HbA1c%	<7.0	<=6.5	<=6.5	<=7.0

Table 1: Basal Insulin Titration Algorithms from World Medical Societies

*a Fasting blood glucose (FBG) target recommendation from the American Association of Clinical Endocrinologists (AACE) 2011 guidelines

DISCUSSION

Although the pathogenesis of type 2 diabetes is mainly due to insulin resistant, but most of T2DM patients (at least 50%) will require insulin because of beta cell dysfunction. Insulin requirement is due to failure of oral anti-diabetic drugs (OADs) to maintain good glycemic control , at the diagnosis of type 2 diabetes in the presence of metabolic decompensation and/or glycosylated hemoglobin > 9.0%, or in the setting of decompensated renal or hepatic insufficiency, myocardial infarction, stroke, acute severe illness, or major surgery (Sanlioglu et al., 2013)

For patients with T2DM, those fail to get good glycemic control with OADs , ADA/EASD recommend to add basal insulin , like NPH(neutral protamine Hagedorn) insulin , insulin glargine or detemir insulin ,starting with low dose (0.1–0.2 U kg/day) and titration according to blood glucose level (Rubino A et al2007), (Arnolds et al., 2013)

Insulin initiation, alone or in combination with OADs, should be started sooner and not later to achieve target A1c, by controlling fasting and postprandial glucose lead to long term glycemic control. Use of a basal insulin reduces glucotoxicity by normalizing fasting glucose, and helps to preserve beta-cell function (Rosenstock, 2004)

There are different approaches to initiate insulin including, basal bolus regimen with step wise intensification of insulin, multiple daily injections approach in which short acting insulin before meal will be added to basal bolus insulin (Byung-Wan et al., 2017)

There are many studies for adding basal insulin to achieve the recommended HbA1c targets in T2DM patients inadequately controlled with oral hypoglycemic agents (OHA) (Byung-Wan et al., 2017)

Study (reference)	Comparators	Proportion of patients achieving <7%of A1c atrial end
Riddle et al. 2003	NPH insulin	57%
	Insulin glargine	58%
Meneghini et al. 2013	Insulin glargine	53%
	Insulin detemir	38%
Fritsche et al. 2010	Basal bolus (glargine/glulisine)	48%
	Biphasic (NPH/RI or NPH/aspart)	28%
Buse et al. 2009	Biphasic (Lispro Mix 75:25)	48%
	Insulin glargine	40%
Liebl et al. 2009	Basal-bolus (detemir/aspart)	60%
	Biphasic (aspart 30:70)	50%

Table 2: showing the proportion of patients achieving HbA1c ≤ 7% at study end across several trials

*Strict glycemic control increases the risk of hypoglycemia, so the balance is needed the two conditions (Vora et al., 2015)

There are several barriers to initiation of insulin therapy. For patients, barriers include fears of injections and hypoglycemia, perceptions that use of insulin will impose life-style restrictions, and the beliefs for some patients that insulin use means that the disease is severe and no hope for management .

Physician's barriers to start insulin therapy include fear of potential side effects of insulin, hypoglycemia and weight gain (Rubino et al., 2007)

The major benefit of basal insulin plus oral anti-diabetic regimen is its simplicity and safety, with the option of step-wise intensification, compared to basal –bolus regimen with multiple injections.

The American Diabetes Association consider HbA1c as an important indicator of long-term glycemic control, and a reliable measure of chronic hyperglycemia and correlates well with the risk of long-term diabetes complications. United Kingdom Prospective Diabetes Study (UKPDS) provide strong evidence that reducing glycated haemaglobin (HbA1c) improves long- term prognosis in terms of diabetic complications (UKPDS study 16).

The UKPDS showed that intensive blood sugar control is associated with significant reduction in macro vascular complication, so 1% reduction of A1c level will lead to 10% reduction in myocardial infarction, and 16% reduction in stroke (Laakso, 1999)

In this study adding basal insulin to oral anti-diabetic drugs showed significant change in glycemic control ,as shown by the difference between preA1c and postA1c %, without adverse effects as hypoglycemia.

CONCLUSION

The addition of basal insulin to oral anti-diabetic medication in uncontrolled insulin-naïve type 2 diabetic patients resulted in significant improvement of glycemic control, with improved HbA1c level, without adverse effects.

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