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Glycosylated hemoglobin level and number of oral antidiabetic drugs predict whether or not glycemic target is achieved in insulin-requiring type 2 diabetes

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ABSTRACT

Aims: Factors predicting success (glycosylated hemoglobin (A1C) < 7%) with insulin therapy in patients with insulin-requiring type 2 diabetes need to be identified.
Methods: A retrospective, multi-center, observational study was conducted for outpatients with oral antidiabetic drug (OAD)-treated type 2 diabetes whose A1C levels remained above 7%. Patients were begun on basal insulin between January 2005 and December 2006. Biochemical variables and demographic data were collected before and after 52 weeks of insulin therapy.
Results: A total of 565 patients (age, 60.4 ± 11.9 years; A1C levels, 10.11 ±1.81%; duration of diabetes, 11.5 ± 6.8 years) were studied. By study end, 63 patients (11.2%) had achieved the glycemic goal (A1C < 7%). The glycemic goal attainment rate was only 9.1% in patients with

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A1C > 8.8% and who were taking >2 OADs at baseline. The highest rate (32.7%) of successful glycemic control was observed in the group of patients with A1C ≤ 8.8% and who used ≤ 2 OADs at baseline.

Conclusions: Insulin-naïve diabetic patients with A1C > 8.8%, especially those who are taking >2 OADs, have small chance to achieve good glycemic control with adding only basal insulin therapy.

1. Introduction

Type 2 diabetes mellitus (DM2) is a progressive disease with multiple metabolic derangements. Achieving a nearly normal glycosylated hemoglobin (A1C) level is associated with improved long-term outcomes and reduced diabetic complications [1]. Although the American Diabetes Association (ADA) has recommended a target A1C level of below 7% [2], most patients with diabetes do not achieve it [3]. When the target level cannot be satisfactorily achieved with oral antidiabetic drugs (OADs), most patients will require insulin therapy because the progressive decline in ß-cell function leads to deterioration in glycemic control [4].

Insulin therapy is considered to be the most effective therapy for the reduction of high glucose levels. However, two systematic reviews of randomized controlled trials that assessed the effectiveness of insulin regimens have indicated that the glycemic target (A1C < 7%) is achieved in only 35–54% of DM2 patients [5,6]. Some observational studies have even shown that a substantial proportion of DM2 patients do not respond to insulin treatment alone or in combination with OADs in a real-world setting [7–9]. Age [10,11], body mass index [10,11], A1C at baseline [10–12] and delay in adding insulin to OADs [13] have all been reported to influence glycemic control in DM2 patients being treated with insulin. Although these studies discuss the factors, they do not suggest any method of improving achievement of glycemic targets in real-world practice. In addition, most physicians and patients will agree to start with basal insulin when beginning insulin therapy. The objective of this study, therefore, was to identify predictors of glycemic target achievement in DM2 patients who had failed to achieve their targets with OADs and who had then been started on basal insulin therapy, and to consider possible approaches to achieving glycemic targets.

2. Methods

2.1. Study population

This study included patients with DM2 who visited the diabetic clinic in the Endocrine and Metabolism Division from 7 diabetic care centers in different areas of Taiwan. All these patients remained treated at these centers from January 2004 to December 2007 and they had received concurrent OAD therapy for more than 1 year. These subjects had failed to achieve optimal glycemic targets with oral agents, as judged by their physicians, and had begun basal insulin therapy between January 2005 and December 2006. We excluded (1) patients diagnosed with type 1 diabetes or gestational diabetes, (2) subjects with baseline A1C level <7% before initiation of insulin therapy, and (3) subjects on insulin other than a basal insulin regimen. In this study, basal insulin regimen was defined as intermediate-acting human insulin or long-acting insulin analog either once or twice daily.

2.2. Study protocol

In this 12-month retrospective, observational study, A1C and fasting plasma glucose levels of all patients were measured within 3 months before they began basal insulin therapy and then within 3 months after 52 weeks of insulin therapy. Other data collected were age, sex, body weight and height, duration of diabetes, type of OAD before insulin therapy and at study end, as well as type and dosage of insulin. Duration of diabetes was defined as the period of time in years from when the patient was diagnosed with diabetes to when he or she was recruited into the study. Patients were defined as having hypertension if they were receiving antihypertensive medications or if systolic blood pressure was ≥140 mmHg or if diastolic blood pressure was ≥90 mmHg. Patients were defined as having dyslipidemia if triglycerides were ≥1.7 mmol/L and/or high-density lipoprotein cholesterol <1.04 mmol/L (<1.29 mmol/L for women), and/or total cholesterol ≥5.18 mmol/L, and/or low-density lipoprotein cholesterol ≥3.37 mmol/L. Those receiving lipid-lowering treatment were also classified as dyslipidemic. The other concomitant disorders associated with diabetes were based on the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) code. They included diabetic microvascular complications, including diabetic retinopathy and blindness (250.5, 362.0, 369), diabetic nephropathy and chronic kidney disease (250.4, 581.81, 583.81, 585), and diabetic macrovascular complications, including cerebral vascular disease (430–438), coronary arterial disease (410–413) and peripheral arterial disease of the foot (250.7, 443.81, 785.4).

2.3. Statistical analysis

All data are presented as mean ± standard deviation. The independent Student's *t*-test was used to analyze continuous data and the chi-square test was used to analyze categorical variables. The demographic variables and factors prior to insulin therapy of patients who continued with basal insulin were included in multivariate logistic regression analysis. ANOVA was used to further analyze A1C quartiles and number of OADs