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Glycemic control and adherence to basal insulin therapy in Taiwanese patients with type 2 diabetes mellitus

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ABSTRACT

Aims/Introduction: The aim of the present study was to assess the glycemic control, adherence and treatment satisfaction in a real-world setting with basal insulin therapy in type 2 diabetes patients in Taiwan.

Materials and Methods: This was a multicenter, prospective, observational registry. A total of 836 patients with type 2 diabetes taking oral antidiabetic drugs with glycated hemoglobin (HbA1c) >7% entered the study. Basal insulin was given for 24 weeks. All treatment choices and medical instructions were at the physician's discretion to reflect real-life practice.

Results: After 24-week treatment, 11.7% of patients reached set HbA1c goals without severe hypoglycemia (primary effectiveness end-point). HbA1c and fasting blood glucose were significantly decreased from (mean ± SD) 10.1 ± 1.9% to 8.7 ± 1.7% (–1.4 ± 2.1%, $P < 0.0001$) and from 230.6 ± 68.8 mg/dL to 159.1 ± 55.6 mg/dL (–67.4 ± 72.3 mg/dL, $P < 0.0001$), respectively. Patients received insulin therapy at a frequency of nearly one shot per day on average, whereas self-monitoring of blood glucose was carried out approximately four times a week. Hypoglycemia was reported by 11.4% of patients, and only 0.7% of patients experienced severe hypoglycemia. Slight changes in weight (0.7 ± 2.4 kg) and a low incidence of adverse drug reactions (0.4%) were also noted. The score of 7-point treatment satisfaction rated by patients was significantly improved by 1.9 ± 1.7 ($P < 0.0001$).

Conclusions: Basal insulin therapy was associated with a decrease in HbA1c and fasting blood glucose, and an improved treatment satisfaction. Most patients complied with physicians' instructions. The treatment was generally well tolerated by patients with type 2 diabetes, but findings pointed out the need to reinforce the early and appropriate uptitration to achieve treatment targets.

INTRODUCTION

The diabetes epidemic is a global problem. The number of people with diabetes aged 20–70 years is expected to increase from 285 million in 2010 to 438 million in 2030[1] as a result of the

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aging population and the prevalence of obesity[2,3]. A retrospective study in Taiwan showed that its prevalence increased from 4.7% to 6.5% for men and from 5.3% to 6.6% for women from 1999 to 2004[4]. This pattern has been repeated across Asia with a three- to fivefold increase over the past 30 years, and more rapidly than that in Western countries[5,6].

Type 2 diabetes is a chronic and progressive disease that leads to many macrovascular and microvascular complications[7]. Optimal glycemic control is fundamental to managing diabetes. Multiple oral antidiabetic drugs (OAD) and insulin therapy might be required to achieve and maintain glycemic goals[8]. It was shown that intensive glycemic control was beneficial in preventing the morbidity related to diabetes in numerous studies including the UK Prospective Diabetes Study[9–13].

However, the majority of patients with long-standing diabetes remained uncontrolled with oral agents. Insulin is the most effective at lowering hyperglycemia, but initiation was often delayed[14,15]. Insulin is usually started in response to elevated glycated hemoglobin (HbA1c) after failure on maximum OADs.[16,17]

The statement of the American Diabetes Association and the European Association for the Study of Diabetes (ADA/EASD) emphasized the importance of the timely addition of basal insulin in patients with type 2 diabetes after OAD[18,19]. The clinical trials showed that the use of basal insulin as an add-on to OAD in patients with type 2 diabetes achieved 7% HbA1c, and approximately half of the patients experienced symptomatic hypoglycemia[20–24]. However, in real-world practice, a retrospective USA study and two prospective studies in Ireland and Japan found that approximately just 20% of the patients taking basal insulin could achieve HbA1c <7% with a low rate of hypoglycemia[16,25,26]. Although some potential reasons for the gap were discussed, data for insulin adherence and frequency of self-monitoring of blood glucose (SMBG) were not reported in these studies. In addition, patient-reported treatment satisfaction is also an important outcome in type 2 diabetic patients receiving insulin therapy[27]. However, the information for patient-reported treatment satisfaction is still limited in past observational studies.

In order to further characterize the outcomes associated with basal insulin therapy in a real-world setting, the present study aimed to discover the glycemic control, treatment adherence, SMBG frequency and patient-reported treatment satisfaction in type 2 diabetic patients after 24 weeks of basal insulin therapy in Taiwan.

MATERIALS AND METHODS

Study design

This was a multicenter and observational registry carried out at 17 centers in Taiwan from 2010 to 2012. The study aimed to investigate the glycemic control, adherence and treatment satisfaction of basal insulin therapy in type 2 diabetes patients. The 24-week period included three visits, on day 0, week 12 and week 24. The OAD and basal insulin were used and adjusted by the physicians according to routine practice.

Participants

Type 2 diabetes patients, who were treated with OAD for at least 24 weeks and had inadequate glycemic control (HbA1c >7%) were enrolled, and received the basal insulin therapy per clinical practice. Patients were ineligible if they were suffering from type 1 diabetes; had been prescribed temporary insulin treatment for gestational diabetes, pancreatic cancer or surgery; not willing to comply with the observational plan; and female patients who were pregnant, breast-feeding or had the intention of becoming pregnant. At baseline, 836 eligible patients were recruited. The retention rate at week 12 and week 24 was 91.6% (766 patients) and 84.2% (704 patients), respectively.

End-points

The primary end-point was the rate of achieving treatment success (achievement of individual HbA1c target without severe hypoglycemia) after 24 weeks. Other endpoints included: (i) achievement rates of individual treatment goals of HbA1c and fasting blood glucose (FBG) predefined by physicians; (ii) change in HbA1c and FBG from baseline; (iii) adherence rate; (iv) frequency of hypoglycemia; (v) change in bodyweight; and (vi) treatment satisfaction.

Glycemic targets were set according to ADA guidelines: (i) HbA1c <7% was set for non-pregnant adults; (ii) stringent HbA1c goals (<6.5%) were set for those who achieved goals without potential hypoglycemia or other adverse effects (i.e., patients with short duration of diabetes, long life expectancy and no significant cardiovascular disease); and (iii) less stringent HbA1c goals (over <8%) were set for patients with histories of severe hypoglycemia, limited life expectancy, advanced microvascular/macrovascular complications, extensive comorbid conditions, and long-standing diabetes for which is difficult to attain goals despite appropriate glucose monitoring and multiple glucose-lowering agents.

Assessments

The effectiveness was evaluated based on HbA1c and FBG values. Results were also analyzed in HbA1c subgroups sorted by four quartiles according to baseline HbA1c. Other data included physical examinations, SMBG frequencies for fasting glucose, treatment adherence, adverse drug reactions (ADRs), hypoglycemia, and treatment satisfaction (a 7-point scale ranging from 7 [satisfied] to 1 [dissatisfied]) assessed by patients.

Safety

Safety was monitored based on ADRs and hypoglycemia. Mild to moderate hypoglycemia was defined as episodes with no need for assistance. Severe hypoglycemia was defined as requiring assistance with blood glucose <56 mg/dL or without blood glucose measurement, but the recovery was attributable to the restoration of blood glucose to normal.

Statistical analysis

Assuming that 26.6% of patients would reach target HbA1c without hypoglycemia[28], and that 15% of patients would be non-evaluable, enrollment of 1,000 patients would provide a precision of 2.9% in the calculation of the 95% confidence interval (CI).

Statistical analysis was based on the number of evaluable patients. Data were summarized using mean, standard deviation (SD), range for continuous parameters and counts/percentages for categorical parameters. Two-sided 95% CI of the difference was calculated. The quantitative variables were compared by the analysis of variance and Student's paired *t*-test. Qualitative variables were compared using Fisher's exact tests or χ^2-tests.

All statistical tests were carried out using two-tailed tests at 5% level of significance; analyses were carried out with SAS software version 9.3 (SAS Institute, Cary, NC, USA).

RESULTS

Baseline characteristics

Across 17 hospitals, a total of 836 patients were enrolled, with a mean age of 62.2 ± 12.4 years, a mean weight of 66.3 ± 13.0 kg, a mean height of 160.7 ± 8.5 cm and an equal sex distribution (Table 1). At baseline, the mean HbA1c and FBG were 10.1 ± 1.9% and 230.6 ± 68.8 mg/dL, respectively. All patients showed a mean diabetes duration of 11.6 ± 7.0 years, and a mean OAD therapy duration of 10.7 ± 6.6 years. Just 57 (6.9%) patients had received insulin therapy before participation, but it had been interrupted for 3.2 ± 2.9 years on average. More than 60% of patients with type 2 diabetes were affected by comorbid dyslipidemia (67.8%) or hypertension (64.3%). The most frequently reported complication was diabetic neuropathy (22.2%), followed by diabetic nephropathy (21.8%) and diabetic retinopathy (20.0%).

Table 1 | Baseline characteristics

Characteristics	Evaluable population (*n* = 836)
Mean age (years)	62.2 ± 12.4
Male, *n* (%)	413 (50.1)
Female, *n* (%)	412 (49.9)
Mean weight (kg)	66.3 ± 13.0
Mean height (cm)	160.7 ± 8.5
Mean diabetes duration (years)	11.6 ± 7.0
Mean OAD duration (years)	10.7 ± 6.6
Previous insulin therapy	
No. patients (%)	57 (6.9)
Mean interruption (years)	3.2 ± 2.9
Complications, *n* (%)	
Diabetic neuropathy	184 (22.2)
Diabetic nephropathy	180 (21.8)
Diabetic retinopathy	166 (20.0)
Comorbidities, *n* (%)	
Dyslipidemia	561 (67.8)
Hypertension	529 (64.3)
Coronary artery disease	100 (12.1)
Stroke	32 (3.9)
Vascular disorder	13 (1.8)
Mean HbA1c (%)	10.1 ± 1.9
Mean FBG (mg/dL)	230.6 ± 68.8

The percentages were calculated based on the number of patients with evaluable data rather than the total eligible population. FBG, fasting blood glucose; HbA1c, glycated hemoglobin; OAD, oral antidiabetic medications.

Prescribed OAD and insulin

Various types of basal insulin were given with OAD at baseline (Table 2). The most frequently prescribed OAD was fixed dose combination–sulfonylurea/metformin (41.0%), followed by sulfonylurea (40.1%) and metformin (33.4%). Most patients were treated with long-acting insulin (insulin glargine 98.9%, insulin detemir 0.4%), whereas intermediate-acting insulin (i.e., neutral protamine Hagedorn insulin) was used in just 0.7% of patients. Premixed insulin was only prescribed at post-therapy visits to a small population (0.9–1.2%).

During the 24-week treatment, the majority of patients continued with the OAD and insulin therapy prescribed at baseline. The population with changes in OAD (either medication or dose) was less than 10%. Just 6.0–7.7% of the patients taking fixed dose combination–sulfonylurea/metformin had changes, whereas that for sulfonylurea and metformin was 5.5–8.7% and 2.8–3.9%, respectively. Similarly, no significant changes in insulin therapy were noted. Insulin glargine was still given to most of the patients (week 12 98.6%, week 24 98.3%).

Patients received insulin glargine at a mean dose of 12.2 ± 5.3 U, whereas that for neutral protamine Hagedorn insulin and insulin detemir were 10.7 ± 5.3 U and 14.0 ± 1.7 U, respectively. Approximately 60% of the patients were asked to adjust the dosage every week, whereas one-quarter of the patients were asked to carry out the titration every 3 days. Two units per adjustment was mostly instructed (39.5% of patients), followed by one unit (24.6% of patients). Insulin glargine, which was used in the majority of the patients, was uptitrated from 12.2 U to 17.7 U during the 24-week treatment. A slight dose escalation was also noted in other basal insulin (Table 2).

Glycemic targets

At baseline (Table 1), the mean HbA1c and FBG were 10.1 ± 1.9% and 230.6 ± 68.8 mg/dL, respectively. Owing to each individual's condition, the treatment targets set by the physicians were HbA1c <7% for 94.2% of patients, and FBG 90–130 mg/dL for 94.6% of patients. The others were asked to reach individualized HbA1c targets of <6.5%, <8%, <9%, <11% or <13.5% based on the physician's discretion.

Effectiveness

After the 24-week basal insulin therapy, an increase in the proportion of patients reaching treatment goals was observed in every aspect (Table 3). The treatment success rate, defined as the proportion of reaching set HbA1c goals without severe

Table 2 | Summary of oral antidiabetic medications and insulin

	Baseline	Change at week 12†	Change at week 24†
OAD, *n* (%)			
Sulfonylurea/metformin‡	343 (41.0)	59 (7.7)	42 (6.0)
Sulfonylurea	335 (40.1)	67 (8.7)	39 (5.5)
Metformin	279 (33.4)	30 (3.9)	20 (2.8)
Dipeptidyl peptidase-4 inhibitor	183 (21.9)	50 (6.5)	22 (3.1)
Alpha-glucosidase inhibitor	159 (19.0)	45 (5.9)	34 (4.8)
Thiazolidinedione	88 (10.5)	34 (4.4)	2 (0.3)
Glinides	77 (9.2)	14 (1.8)	14 (2.0)
Thiazolidinedione/metformin‡	8 (1.0)	9 (1.2)	2 (0.3)
Dipeptidyl peptidase 4 inhibitor/metformin‡	1 (0.1)	1 (0.1)	0 (0.0)
	Baseline	week 12	week 24
Insulin, *n* (%)			
Insulin glargine	827 (98.9)	709 (98.6)	646 (98.3)
NPH insulin	6 (0.7)	2 (0.3)	2 (0.3)
Insulin detemir	3 (0.4)	0 (0.0)	1 (0.2)
Insulin aspart	0 (0.0)	1 (0.1)	1 (0.3)
Biphasic insulin aspart 70/30	0 (0.0)	6 (0.8)	5 (0.8)
Insulin lispro	0 (0.0)	1 (0.1)	0 (0.0)
Insulin lispro 75/25	0 (0.0)	0 (0.0)	1 (0.2)
Insulin lispro 50/50	0 (0.0)	0 (0.0)	1 (0.2)
Mean dose (IU)			
Insulin glargine	12.2 ± 5.3	16.2 ± 8.5	17.7 ± 10.0
NPH insulin	10.7 ± 5.3	9.0 ± 1.4	15.0 ± 7.1
Insulin detemir	14.0 ± 1.7	NA§	16.0 ± NA§

The percentages were calculated based on the number of patients with evaluable data rather than the total eligible population. †Results on oral antidiabetic medications (OAD) at week 12 and week 24 present the population with changes in OAD (change in dose or change to the listed OAD). ‡Fixed dose combination. §At week 12, no patients ($n = 0$) were taking insulin detemir, and at week 24, there was one patient ($n = 1$) taking insulin detemir. NA, not applicable; NPH, neutral protamine Hagedorn.

hypoglycemia (primary effectiveness endpoint), was 8.1% at week 12 and 11.7% at week 24 (95% CI 9.38–14.53%). The rate of reaching HbA1c <7% at week 12 and week 24 was 6.9% and 10.7%, respectively. HbA1c levels were significantly decreased to 8.9 ± 1.6% (−1.1 ± 1.9%) and 8.7 ± 1.7% (−1.4 ± 2.1%) at week 12 and week 24 (both $P < 0.0001$), respectively (Table 4). Similarly, the mean FBG levels were significantly reduced to 159.1 ± 55.6 mg/dL (−67.4 ± 72.3 mg/dL) at study end ($P < 0.0001$).

HbA1c subgroups analysis

The treatment responses were summarized by four quartiles of baseline HbA1c (Table 5). The highest achievement rate was observed in the Q1 group (HbA1c/FBG: 16.8%/38.8%). However, the greatest changes in HbA1c/FBG were noted in the Q4 group (−3.1%/−102.2 mg/dL).

Weight

A slight increase of 0.7 ± 2.4 kg in weight at week 24 was detected ($P < 0.0001$). The profiles were comparable among patients given different types of insulin (insulin glargine 0.6–0.9 kg, insulin detemir/neutral protamine Hagedorn insulin 0.5–0.9 kg).

Adherence

Approximately 99.5% of the patients were instructed to administer insulin therapy once daily (0.5% of the patients: twice daily). The treatment adherence was good over the period. The number of insulin administrations was 83.1 ± 22.4 between baseline to week 12 and 84.6 ± 25.0 between week 12 to week 24, overall yielding the frequency of nearly one shot per day. Approximately 91.6% and 92.5% of patients at week 12 and week 24 had received daily insulin injection in the past week (7 days) just before the upcoming visit, respectively. Almost all the patients (99%) were instructed to carry out SMBG, and mostly at a frequency of daily or three times a week. Under the assessment of physicians, 87.4% of the patients complied with SMBG instructions. The total number of SMBG was 48.2 ± 34.5 at week 12 and 41.4 ± 33.7 at week 24, giving the frequency of approximately four SMBGs per week.

Satisfaction

A significant increase in treatment satisfaction was noted from 3.2 ± 1.6 at baseline to 5.2 ± 1.3 at week 24 (+1.9 ± 1.7, $P < 0.0001$). The main reasons for not achieving treatment

Table 3 | Summary of treatment goal achieving rate

	Achieved	Achieved without severe hypoglycemia	Achieved without any hypoglycemia	HbA1c <6.5%	HbA1c <7%	FBG <130 mg/dL
Week 12						
Achieved, *n* (%)	53 (8.3)	52 (8.1)	47 (7.3)	13 (2.0)	45 (6.9)	236 (33.7)
Not achieved, *n* (%)	588 (91.7)	589 (91.9)	594 (92.7)	638 (98.0)	606 (93.1)	465 (66.3)
Week 24						
Achieved, *n* (%)	72 (11.9)	71 (11.7)	59 (9.7)	19 (3.1)	66 (10.7)	208 (32.3)
Not achieved, *n* (%)	534 (88.1)	535 (88.3)	547 (90.3)	597 (96.9)	550 (89.3)	436 (67.7)

The percentages were calculated based on the number of patients with evaluable data rather than the total eligible population. FBG, fasting blood glucose; HbA1c, glycated hemoglobin.

Table 4 | Summary of glycated hemoglobin and fasting blood glucose

	n	Mean ± SD	Change (*n*)	Change ± SD	*P*-value
HbA1c (%)					
Baseline	836	10.1 ± 1.9			
Week 12	651	8.9 ± 1.6	651	−1.1 ± 1.9	<0.0001*
Week 24	616	8.7 ± 1.7	616	−1.4 ± 2.1	<0.0001*
FBG (mg/dL)					
Baseline	810	230.6 ± 68.8			
Week 12	679	160.9 ± 57.7	662	−66.6 ± 73.2	<0.0001*
Week 24	619	159.1 ± 55.6	600	−67.4 ± 72.3	<0.0001*

**P*-value by paired *t*-test, statistically significant; *n* is the number of patients with evaluable data. FBG, fasting blood glucose; HbA1c, glycated hemoglobin.

Table 5 | Treatment response at week 24

HbA1c (%)	Baseline HbA1c			
FBG (mg/dL)	Q1 (7.1–8.6%)	Q2 (8.7–9.7%)	Q3 (9.8–11%)	Q4 (11.1–19.1%)
No. patients	170	183	169	176
HbA1c <7%, *n* (%)	23 (16.4)	16 (10.4)	12 (8.3)	9 (6.2)
Mean HbA1c	8.1 ± 0.4	9.2 ± 0.3	10.3 ± 0.4	12.5 ± 1.5
Mean HbA1c change	−0.1 ± 1.4	−0.8 ± 1.4	−1.6 ± 1.7	−3.1 ± 2.2
FBG <130 mg/dL, *n* (%)	58 (38.9)	46 (30.5)	47 (31.2)	32 (22.5)
Mean FBG	187.5 ± 51.8	211.4 ± 52.1	238.4 ± 57.8	276.8 ± 58.8
Mean FBG	−38.0 ± 56.8	−55.0 ± 67.5	−75.5 ± 67.6	−104.7 ± 75.1

The percentages were calculated based on the number of patients with evaluable data rather than the total eligible population. FBG, fasting blood glucose; HbA1c, glycated hemoglobin.

targets were insufficient uptitration (36.2%), non-compliance with the treatment (20.3%) and lack of effectiveness (18.6%).

Hypoglycemia

The overall incidence of hypoglycemia was 11.4% (87/836). A decrease in incidence was noted between week 12 and week 24, changing from 8.6% to 5.2%. Most of the events were mild-to-moderate. Just six patients experienced severe hypoglycemia.

Safety

Just four non-serious ADRs were reported in three patients (0.4%). Three ADRs were mild in severity, and one ADR (flushing/sweating) that occurred in one patient receiving insulin glargine was considered to be severe and drug-related. No other clinically relevant changes in physical examination, vital signs and laboratory variables were noted.

DISCUSSION

The present multicenter, prospective, observational registry for Taiwanese patients with type 2 diabetes inadequately controlled on OAD showed that significant reductions in HbA1c and FPG were seen after 24 weeks of basal insulin therapy in real-world practice. The rate of hypoglycemia was low, and the bodyweight gain was minimal.

In general, achieving and sustaining the HbA1c target goal at lower than 7% was recommended by the diabetes guidelines[29–33]. Most of the patients (94%) in this registry would like to achieve HbA1c goal <7%. However, just 10.7% of patients reached HbA1c <7% at week 24. Even in the patients with HbA1c ≤8.6% at baseline, just 16.4% of them could reach the HbA1c target of <7%. The patient-reported treatment satisfaction was significantly improved after basal insulin therapy, and most patients complied with physicians' instructions for insulin injections and SMBG. Therefore, achieving adequate glycemic control in type 2 diabetes patients with basal insulin has still remained a clinical challenge.

The low HbA1c goal achievement rate (10.7%) in this registry might be attributed to the suboptimal dose of basal insulin therapy. In a Korean registry in insulin-naïve patients, the mean HbA1c was reduced from 9.1% to 7.3% after 6 months of basal insulin therapy, and 47.0% of the patients achieved HbA1c <7%.[34] The mean daily dose of basal insulin in the present study was relatively low (from 0.18 U/kg to 0.26 U/kg), as compared with the Korean study (from 0.26 U/kg to 0.36 U/kg). Furthermore, the type 2 diabetes duration, OAD treatment duration and HbA1c/FBG level in the present study were all higher than those in the Korean study. Such conditions might also contribute to a lack of effectiveness.

The American Association of Clinical Endocrinologists (AACE) guideline recommends a starting daily dose of 0.2–0.3 U/kg for initiation of basal insulin when HbA1c is >8%, which should be adjusted every 2–3 days by two units.[35] In the present study, basal insulin was given at a lower average starting dose (0.18 U/kg), and was not adjusted aggressively within 24 weeks to reach glycemic goals. Insufficient uptitration was also identified as the major factor (36.2%) contributing to the low target achievement rate. It shows the need to reinforce appropriate uptitration.

SMBG is particularly important for patients treated with insulin to monitor for and prevent hypoglycemia and hyperglycemia. Several database studies showed that more frequent SMBG were associated with better metabolic control in diabetic patients treated with insulin[36–38]. The guidelines recommended SMBG three or more times daily for intensive insulin therapy, but the frequency and timing of SMBG should be dictated by the particular needs of the patient[39–41]. The ADA-EASD consensus statement in 2009 recommended checking fasting glucose usually once daily when starting basal insulin therapy in patients with type 2 diabetes[23]. A large-scale survey in the Netherlands[42] showed that there was a wide variation in recommendations on SMBG that were given to patients with type 2 diabetes receiving one or two insulin injections a day of long-acting insulin. Once every 2 weeks was most frequently reported (32–37%), followed by 1 day a week (21–27%) and 1 day a month (21–26%)[42]. The findings in the present study, such as SMBG adherence and slow dose uptitration, might reflect a prudent approach among Taiwanese physicians. An Asian trial of basal insulin reported using a conservative titration goal relative to comparative trials in Western populations owing to a perceived increased risk of hypoglycemia in Asian patients[43]. However, the present study found that the incidence of hypoglycemia was low (week 0–12 8.6%, week 13–24 5.2%), and most episodes were mild-to-moderate. It indicates that more aggressive dose titration of basal insulin might help more patients to reach treatment goals.

Weight gain has been known to be a barrier to using insulin therapy in type 2 diabetes patients[44]. In general, an increase in weight was widely recognized during the first year of insulin therapy (+2 to 6 kg)[45,46]. However, weight gain after 6-month insulin therapy was minimal in the present study (+0.7 ± 2.4 kg), as compared with previous trials[20,47]. The overall safety profile was favorable (low incidence of ADRs/hypoglycemia and minimal weight gain).

Given the progressive nature of this disease, characterized by gradual impairment in β-cell function and loss of β-cell mass[48], most type 2 diabetes patients require insulin therapy. According to the ADA guideline and ADA/EASD consensus statement[19,40], in general, HbA1c goal should be achieved and sustained at the level of <7%, and insulin could be initiated when HbA1c is not at goal. However, the present results showed that insulin therapy in Taiwan was delayed. This study comprised of patients with poorly controlled type 2 diabetes, with a mean HbA1c of 10.1% at baseline (diabetes duration 11.6 ± 7.0 years, OAD therapy duration 10.7 ± 6.6 years). Most of the patients were naïve to insulin therapy, just 6.9% of them had received insulin therapy before participation.

Considering the type 2 diabetes management in Taiwan, several factors might attribute to the delayed insulin therapy. Insulin usually acts as the last choice when finding no other oral agents can effectively manage the condition. A major challenge is to initiate insulin therapy in a timely manner when HbA1c is not high. The technical difficulty of insulin therapy (subcutaneous injection and regular SMBG) might actually reduce patients' willingness to accept insulin therapy. Often, patients have misperceptions about insulin therapy. Insulin initiation can sometimes cause patients to feel that they are punished for having poor control of diabetes. Physicians, patients and healthcare teams should carefully overcome psychological barriers, and work closely to control glucose levels.

Suboptimal titration of basal insulin might be partly related to the concern of hypoglycemic risk of rapid improvement in glycemic control. Therefore, the classic mantra, "Start low, and go slow" holds true here. These insights point towards the need to reinforce the importance of appropriate uptitration to achieve treatment targets. More meticulous and aggressive titration is important to enable more patients to achieve treatment targets.

In conclusion, the present study carried out in Taiwanese patients with type 2 diabetes showed that: (i) treatment of basal insulin therapy for 6 months significantly reduced HbA1c/FBG values, and was tolerated by patients without serious safety concern; (ii) most of the patients complied with physicians'

instructions and were satisfied with the treatment; and (iii) more meticulous titration might enable more patients to achieve treatment targets. Insulin glargine is used for insulin initiation in the majority of patients in an outpatient setting in Taiwan, and reflects the physician behaviors. Although there were potential limitations to the registry, they reflected the real-world clinical practice in Taiwan, which was the key aim of the present study.

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DISCLOSURE

Bill Chen is an employee of Sanofi. All other authors were involved in the conduct of the study as investigators. No additional known conflicts of interests exist and no honoraria were offered or received for co-author participation in the writing of the present report.

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