Endokrynologia Polska
DOI: 10.5603/EP.a2018.0037
Tom/Volume 69; Numer/Number 4/2018
ISSN 0423–104X

Dose titration model and correlative factors analysis in Chinese patients with type-2 diabetes on basal insulin — results from an Observational Registry of Basal Insulin Treatment study

Model dostosowywania dawki i analiza czynnika współzależnego u chińskich pacjentów z cukrzycą typu 2 leczonych podstawową dawką insuliny — wyniki badania ORBIT (*Observational Registry of Basal Insulin Treatment*)

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Abstract

Introduction: This study evaluates an insulin dose titration model and factors that impact insulin dose adjustment in Chinese adults with type-2 diabetes, who receive basal insulin in real-world settings.

Material and methods: A total of 19,894 patients from the ORBIT study were included. These patients were divided into four groups, according to the type of insulin dose adjustment: no insulin titration (group A), self-titration (group B), physician-led insulin titration (group C), and combined physician and patient-led insulin titration (group D). Data were collected and compared at baseline and after six months of treatment.

Results: A total of 12,865 patients completed the visits and were included in the analysis. Among these patients, 3187 (24.8%), 1971 (15.3%), 5165 (40.1%), and 2542 (19.8%) patients were included in groups A, B, C, and D, respectively. The multivariate logistic regression analysis revealed that the duration of diabetes, body mass index, microvascular complications, inpatient days, HbA1C level, and self-monitoring of blood glucose (SMBG) were positively correlated with insulin titration in group B, C, and D, compared with group A. The number of inpatient days and outpatient visits were positively correlated with dose adjustment for physician-led titration, while this was negatively correlated for self-titration. Self-titration encouraged by physicians and home blood glucose monitoring were positively correlated with self-titration and the combined physician and patient-led titration.

Conclusions: High HbA1C level, SMBG, long disease duration, microvascular complications, and the encouragement of physicians while initiating insulin use prompt patients to perform dose adjustments in real-world settings. **(Endokrynol Pol 2018; 69 (4): 395–402)**

Key words: *type 2 diabetes, basal insulin therapy, diabetes education, real-world settings, ORBIT study*

Streszczenie

Wstęp: Badanie ma na celu ocenę modelu dostosowywania dawki insuliny i czynników, mających wpływ na dostosowanie dawki insuliny u chińskich dorosłych pacjentów z cukrzycą typu 2 leczonych podstawową dawką insuliny w warunkach rzeczywistych.

Materiał i metody: W badaniu udział wzięło 19 894 pacjentów z badania ORBIT, którzy zostali podzieleni na 4 grupy, w zależności od typu dostosowywania dawki insuliny: brak dostosowywania dawki insuliny (grupa A), samodzielne dostosowywanie dawki (grupa B), dostosowywanie dawki przez lekarza (grupa C) oraz dostosowywanie dawki zarówno przez lekarza jak i przez pacjenta (grupa D). Dane zostały zebrane i porównane na początku badania i po 6 miesiącach leczenia.

Wyniki: Łącznie 12 865 pacjentów ukończyło wizyty i zostało uwzględnionych w analizie. Spośród tych pacjentów, 3187 (24,8%), 1971 (15,3%), 5165 (40,1%) i 2542 (19,8%) badanych włączono odpowiednio do grup A, B, C i D. Wieloczynnikowa analiza regresji logistycznej wykazała, że czas trwania cukrzycy, wskaźnik masy ciała, powikłania mikronaczyniowe, dni hospitalizacji, stężenie HbA1C i samokontrola stężenia glukozy we krwi (*self-monitoring of blood glucose*; SMBG) były dodatnio skorelowane z dostosowywaniem insuliny w grupach B, C i D w porównaniu z grupą A. Liczba dni hospitalizacji i wizyt ambulatoryjnych były dodatnio skorelowane z dostosowywaniem dawek przez lekarza i ujemnie skorelowane z samodzielnym dostosowywaniem dawki. Zachęcanie przez lekarzy do samodzielnego dostosowywania dawki i monitorowanie stężenia glukozy we krwi w warunkach domowych były dodatnio skorelowane z samodzielnym dostosowywaniem dawki oraz dostosowywaniem dawki zarówno przez lekarza, jak i przez pacjenta.

Wnioski: Wysokie stężenie HbA1C, samokontrola stężenia glukozy we krwi, długi czas trwania choroby, powikłania mikronaczyniowe oraz zachęta lekarzy podczas inicjowania podawania insuliny skłaniają pacjentów do dostosowywania dawek w warunkach rzeczywistych. **(Endokrynol Pol 2018; 69 (4): 395–402)**

Słowa kluczowe: *cukrzyca typu 2, podstawowa insulinoterapia, edukacja diabetologiczna, warunki rzeczywiste, badanie ORBIT*

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Introduction

T2DM is one of the most common diseases that endangers public health. A survey conducted by the World Health Organisation in 2011 revealed that the prevalence of diabetes worldwide was 346 million, and according to the International Diabetes Federation, this number is estimated to reach 552 million by 2030, globally. Furthermore, China has been reported to have the highest incidence of diabetes worldwide. In China, the morbidity rate among adult patients with T2DM is approximately 9.8%, in which 92.4 million adults suffer from the disease [1]. T2DM may lead to diabetes-related microvascular complications, which in turn play a major role in exacerbating macrovascular complications. The increasing prevalence of diabetes is expected to pose a heavy economic burden on society, and the adequate glycaemic control of diabetes patients has been shown to be effective in reducing the incidence of diabetes-related complications, especially in the early stages of the disease [2–4]. Thus, several countries, including China, have published diabetes control guidelines that recommend the control of glycated haemoglobin (HbA1C) levels below 7% [5, 6]. Although significant advancements have been made in diabetes drug research in recent years, achieving and maintaining the goal of HbA1C < 7% remains challenging for healthcare providers and patients worldwide. A survey [7] conducted in the US revealed that the rate of achieving good glycaemic control in diabetes patients was 52.9%, while recent studies have shown that this rate was only 39.7% in China [8].

The natural progression of the disease leads to the gradual regression of islet cell function, resulting in an increase in blood glucose. Therefore, to control the blood glucose below a standard level, exogenous insulin treatment is needed when oral medications fail to control the HbA1C level within the compliance range. Guidelines from different countries recommend the use of basal insulin in combination with oral antidiabetes drugs (OADs) to improve glycaemic control [6]. However, in clinical practice, introducing insulin treatment remains challenging. Studies [9, 10] have shown that, overall, 26.9–58.0% of patients across various countries are reluctant to accept insulin treatment, which interferes with the timely initiation of insulin treatment after the onset of hyperglycaemia. On the other hand, another important factor that affects glycaemic control is insulin dose adjustments following insulin treatment initiation. Numerous randomised, controlled clinical studies have confirmed the efficacy and safety of insulin treatment. However, these studies were conducted under the guidance and close observation of a physician. A study [11] conducted in China revealed that in clinical practice, only 27% of T2DM patients controlled their HbA1C below the normal range following insulin treatment initiation. However, at present, no study has assessed actual insulin dose adjustments and the factors that influence dose adjustment in Chinese patients with T2DM. The present study used data from the Observational Registry of Basal Insulin Treatment (ORBIT) study [12], which includes a large sample size, in order to understand the present clinical practice of insulin dose adjustment following the initiation of insulin treatment. In addition, a dose titration model was applied to compare the differences in insulin dose adjustment across various groups at baseline and after six months of treatment. Also, factors that may affect insulin dose adjustment in this model were investigated.

Material and methods

Study objectives

The primary objective of this analysis was to understand the pattern of insulin dose adjustment following basal insulin initiation in clinical practice in T2DM patients using a dose titration model, and to explore the factors that influence insulin dose adjustment following basal insulin initiation in the real world.

Overall design and subjects

Data were collected from patients in the ORBIT study. All participants provided written, informed consent. A total of 19,894 T2DM patients with uncontrolled HbA1C on OADs started using long-acting formulations. These patients were divided into four groups, according to the type of insulin dose adjustment: no insulin titration (group A), self-led insulin titration (group B), physician-led insulin titration (group C), and combined physician and patient-led insulin titration (group D). Patients who stopped using insulin after the baseline visit and those who did not complete the follow-ups were excluded from the analysis. Data were recorded at baseline and at the follow-up visits after initiation of insulin treatment for a period of six months. Differences between the four groups were compared across the follow-up visits. Differences between the clinical data among different groups were also compared at baseline and after six months of treatment. In addition, each group was compared against the no-dose-adjustment group to explore the factors that influence insulin dose adjustment in patients.

Treatments

This was an observational study. None of the selected patients received basal insulin prior to enrolment. The selection of basal insulin formulations and dose adjustments were based on the physician's discretion and the patient's needs.

Data collection and assessments

Data on baseline demographics, education level, diabetes duration, treatment settings (inpatient or outpatient), macrovascular complications, microvascular complications, and HbA1C level were collected. In addition, information on whether the patients performed the self-monitoring of blood glucose (SMBG) at baseline and after insulin treatment for six months, the frequency of SMBG, whether the physicians encouraged patients to adjust their insulin dose, outpatient visits and inpatient days, hypoglycaemia events, HbA1C level, and out-of-pocket costs were recorded, in order to analyse and compare the characteristics of the four dose-adjustment groups. Furthermore, the same information was also recorded during the follow-up visits to determine factors that influence patients to adjust their insulin dose.

Statistics

The study population included patients treated with basal insulin for six months. The characteristics were described for all participants, as well as for the individual groups. Continuous variables with normal distribution were summarised using descriptive statistics, and were presented as mean ± standard deviation (SD) values. Continuous variables of skewed distribution were reported as median and quartile. Discrete variables were presented as n (%). The statistical significance of differences between subpopulations was not reported because the sample was sufficiently large to establish significance. Multinomial logistic analyses were used to assess the independent associations in the insulin titration model.

Results

From December 2011 to June 2013, 19,894 patients with T2DM uncontrolled on OADs began receiving basal insulin [13]. Among these patients, 12,865 patients completed the visits and were included into the analysis. The average age of these patients was 55.7 ± 10.6 years, and 6829 (53.1%) of these patients were male. The average diabetes duration was 6.8 ± 5.3 years. Overall, 3187 (24.8%) patients had no insulin titration (group A), 1971 (15.3%) patients performed self-titration (group B), 5165 (40.1%) patients underwent physician-led insulin titration (group C), and 2542 (19.8%) patients underwent combined physician and patient-led insulin titration (group D). After six months of insulin treatment, 41.7% of patients achieved the target of HbA1C < 7%. Glycated haemoglobin decreased by 2.2%. Among these patients, 48.3%, 36.6%, 40.9%, and 38.8% were from group A, B, C, and D, and glycated haemoglobin decreased by 2.3%, 2.1%, 2.1%, 2.3%, respectively. Furthermore, fasting blood glucose was 7.4 ± 2.2, 8.0 ± 2.5, 7.7 ± 2.4, and 7.8 ± 2.4 mmol/L, while the frequency of hypoglycaemia was 0.2 ± 5.4, 3.2 ± 27.0, 1.8 ± 7.8, and 4.3 ± 12.4 events in groups A, B, C, and D, respectively. No significant difference was noted between groups with regard to severe hypoglycaemia events. Overall, 42.3%, 47.5%, 43.3%, and 49.3% of patients in group A, B, C, and D, respectively, performed home monitoring of blood glucose, and 23.0%, 14.0%, 41.4%, and 21.5% of patients in group A, B, C, and D, respectively, performed SMBG. The frequency of SMBG in group A, B, C, and D was 5.3 ± 10.4, 5.8 ± 11.7, 5.0 ± 9.5, and 5.3 ± 8.5 times during the six-month follow-up period, while the number of hospitalisation days was 0.5 ± 2.9, 0.6 ± 5.1, 0.9 ± 4.6, and 0.9 ± 4.1, respectively, and the number of clinic visits was 4.6 ± 4.2, 4.1 ± 4.2, 6.9 ± 5.5, and 6.2 ± 5.8, respectively. Table I summarises the baseline characteristics and demographics of patients in each group. Table II shows the efficacy and safety variables in the different titration groups.

Multinomial logistic regression analysis revealed that the duration of diabetes, body mass index (BMI), microvascular complications, inpatient treatment, HbA1C level, and SMBG at baseline were positively correlated with insulin titration (Table III).

The number of inpatient days and outpatient visits were positively correlated with dose adjustment in group C but were negatively correlated with dose adjustment in group B. Prior insulin therapy was positively correlated with self-dose titration and combined physician and patient-led dose titration. Compared with group A, the educational degree of patients was negatively correlated with dose adjustment in group C and D, but was positively correlated with dose adjustment in group B. Initial insulin treatment at tertiary hospitals was positively correlated with dose adjustment in group C and D. Encouragement of self-titration by physicians and home blood glucose monitoring were positively correlated with self-titration and combined physician and patient-led titration. The multivariate logistic regression analysis revealed that the level of hospitals where patients started to use insulin, gender, OAD duration, and out-of-pocket costs were not correlated with insulin dose titration, compared with patients without insulin titration.

Discussion

In the present observational study conducted in a real-world clinical setting, after six months of basal insulin treatment, 3187 (24.8%) patients had no insulin titration (group A), 1971 (15.3%) patients performed self-titration (group B), 5165 (40.1%) patients underwent physician-led insulin titration (group C), and 2542 (19.8%) patients

Table I. *Characteristics in different titration groups*
Tabela I. *Charakterystyka różnych grup dostosowywania dawki*

Variables	Overall	A	B	C	D
N	12,865	3187	1971	5165	2542
Hospital level					
— secondary hospital	6855 (53.3%)	1663 (52.2%)	1028 (52.2%)	2779 (53.8%)	1385 (54.5%)
— tertiary hospital	6010 (46.7%)	1524 (47.8%)	943 (47.8%)	2386 (46.2%)	1157 (45.5%)
Gender (male) (%)	6829 (53.1%)	1738 (54.5%)	1089 (55.3%)	2651 (51.3%)	1351 (53.1%)
Age (years)	55.7 ± 10.2	56.1 ± 10.6	55.6 ± 10.1	55.9 ± 10.2	54.9 ± 9.8
— ≥ 60	4770 (37.1%)	1260 (39.5%)	724 (36.7%)	1936 (37.5%)	850 (33.4%)
BMI [kg/m^2]	24.7 ± 3.3	24.6 ± 3.4	24.8 ± 3.4	24.6 ± 3.3	24.8 ± 3.3
Out of pocket	40.6 ± 26.6	38.1 ± 24.7	38.0 ± 26.9	42.3 ± 27.5	42.0 ± 26.4
Education degree					
— primary school or illiterate	3288 (25.6%)	809 (25.4%)	432 (21.9%)	1376 (26.6%)	671 (26.4%)
— junior high school	3949 (30.7%)	940 (29.5%)	558 (28.3%)	1669 (32.3%)	782 (30.8%)
— senior high school	3326 (25.9%)	811 (25.4%)	583 (29.6%)	1285 (24.9%)	647 (25.5%)
— junior college or higher	2302 (17.9%)	627 (19.7%)	398 (20.2%)	835 (16.2%)	442 (17.4%)
Diabetes duration	6.8 ± 5.3	6.5 ± 5.4	7.1 ± 5.6	6.8 ± 5.2	6.9 ± 5.2
OAD Duration	6.0 ± 5.1	5.7 ± 5.1	6.3 ± 5.4	6.0 ± 5.0	6.1 ± 5.1
Patient resource					
— out-patient clinic	5864 (45.6%)	968 (30.4%)	725 (36.8%)	2748 (53.2%)	1423 (56.0%)
— in-patient ward	7001 (54.4%)	2219 (69.6%)	1246 (63.2%)	2417 (46.8%)	1119 (44.0%)
Macro complication	2076 (16.1%)	492 (15.4%)	328 (16.6%)	798 (15.5%)	458 (18.0%)
Micro complication	3814 (29.6%)	925 (29.0%)	674 (34.2%)	1404 (27.2%)	811 (31.9%)
HbA1c	9.5 ± 2.0	9.4 ± 2.0	9.5 ± 1.9	9.6 ± 2.0	9.7 ± 2.0
Encouraged self-titration	4801 (37.3%)	975 (30.6%)	857 (43.5%)	1629 (31.5%)	1340 (52.7%)
Home blood glucose monitor at v1	5773 (44.9%)	1347 (42.3%)	937 (47.5%)	2235 (43.3%)	1254 (49.3%)
Home blood glucose monitor at v3	8398 (65.3%)	1889 (59.3%)	1416 (71.8%)	3191 (61.8%)	1902 (74.8%)
Have SMBG at v1	8692 (67.6%)	2001 (23.0%)	1221 (14.0%)	3600 (41.4%)	1870 (21.5%)
SMBG times at v1 # (times/month)	5.3 ± 9.9	5.3 ± 10.4	5.8 ± 11.7	5.0 ± 9.5	5.3 ± 8.5
Have SMBG at v3	10879 (84.6%)	2454 (77.0%)	1569 (79.6%)	4520 (87.5%)	2336 (91.9%)
SMBG times at v3 # (times/month)	6.5 ± 7.9	5.5 ± 7.4	6.6 ± 8.2	6.5 ± 7.8	7.5 ± 8.4

BMI, body mass index; HbA1C, glycated haemoglobin; OAD, oral antidiabetes drug; SMBG, self-monitoring of blood glucose; #use the nonparametric test — Kruskal--Wallis H test

underwent combined physician and patient-led insulin titration (group D).

In group A 3187 (24.8%) patients did not adjust their insulin dose; the average age of these patients was higher compared to patients in groups B, C, and D. Patient age in the present study was negatively correlated with insulin dose adjustment. A possible reason is that elderly patients were afraid of the incidence of hypoglycaemia, which highlights the need to educate elderly patients on how to adjust insulin usage in order to acquire good glycaemic control and avoid hypoglycaemia. Furthermore, patients who received their first basal insulin treatment in an inpatient setting accounted for the highest proportion of patients in this group compared with groups B, C, and D. HbA1C and fasting plasma glucose levels were lower in this group. Elevated blood glucose level may be a key factor for insulin dose adjustment. The present study revealed that HbA1C level was positively correlated with insulin dose titration. A meta-analysis [14] also revealed that a positive relationship between baseline HbA1C and the magnitude of HbA1C change (which is an indicator of glucose control level) is a key factor for insulin dose adjustment. In addition, fewer patients were encouraged

Table II. *Effect and safety variable description in different titration groups*
Tabela II. *Opis zmiennej efektu i zmiennej bezpieczeństwa w różnych grupach dostosowywania dawki*

Variables	Overall 12,816	A 3171	B 1951	C 5157	D 2537
HbA1c control (< 7%)	5342 (41.7%)	1533 (48.3%)	715 (36.6%)	2109 (40.9%)	985 (38.8%)
HbA1c at v3	7.4 ± 1.3	7.1 ± 1.2	7.5 ± 1.5	7.4 ± 1.3	7.5 ± 1.4
HbA1c v3-v1	–2.2	–2.3	–2.1	–2.1	–2.1
FPG control (< 7 mmol/L)	3867 (45.3%)	995 (51.5%)	433 (40.7%)	1685 (45.0%)	754 (41.9%)
FPG (mmol/L)	7.7 ± 2.4	7.4 ± 2.2	8.0 ± 2.5	7.7 ± 2.4	7.8 ± 2.4
Severe hypoglycaemia	69 (0.5%)	11 (0.3%)	15 (0.8%)	18 (0.3%)	25 (1.0%)
Severe hypoglycaemia times	0.0 ± 0.6	0.0 ± 0.7	0.1 ± 0.7	0.0 ± 0.4	0.1 ± 0.6
Ordinary hypoglycaemia	1186 (9.2%)	133 (4.2%)	204 (10.4%)	402 (7.8%)	447 (17.6%)
Ordinary hypoglycaemia times	2.3 ± 13.3	0.9 ± 5.4	3.2 ± 27.0	1.8 ± 7.8	4.3 ± 12.4
Hospitalised in the past 6 months	696 (5.4%)	144 (20.7%)	78 (11.2%)	314 (45.1%)	16023.0%)
Out-patient clinic in the past 6 months	11 780 (91.6%)	2795 (23.7%)	1686 (14.3%)	4899 (41.6%)	2400 (20.4%)
Hospitalised days	0.8 ± 4.2	0.5 ± 2.9	0.6 ± 5.1	0.9 ± 4.6	0.9 ± 4.1
Out-patient clinic times	5.8 ± 5.2	4.6 ± 4.2	4.1 ± 4.2	6.9 ± 5.5	6.2 ± 5.8

FPG, fasting plasma glucose; HBA1C, glycated haemoglobin

to perform self-titration in this group; it is also one of the reasons of patients did not adjust insulin dose. The present study also revealed that the encouragement of doctors was positively correlated with insulin dose adjustment. A survey [15] conducted in China revealed that poor glucose control was partly correlated with a lack of diabetes education.

The present study revealed that inpatient days and clinic visits were negatively correlated with self-titration. In group B, out-of-pocket costs were low, diabetes duration and OAD use were relatively longer, the rate of microvascular and macrovascular complications was low, and HbA1C control rate and hyperglycaemia and severe hyperglycaemia rates were similar to those in the other three groups. However, clinic visits and inpatient days were lower compared with the other three groups. This finding is inconsistent with the results of the present study, in which patients started using insulin under inpatient treatment settings because inpatient treatment costs can be reimbursed through the Chinese medical insurance system. Therefore, patients prefer starting insulin treatment in the ward instead of self-adjusting their insulin dose. Moreover, patients are sceptical regarding the safety of insulin adjustment when visiting clinics or when self-adjusting their insulin dose. Various randomised controlled studies [16–18] have shown that self-titration of insulin had similar efficacy to physician-led insulin titration. This suggests that it is necessary to instruct patients to conduct self-led insulin titration, which would further strengthen the patient's ability to manage their diabetes. In group B, more patients performed SMBG, compared to the other three groups. SMBG performance and higher frequency of SMBG had a positive effect on insulin dose adjustment in the present study.

Furthermore, in group C 5165 (40.1%) patients adopted physician-led insulin titration. The proportion of out-of-pocket costs and microvascular complications were higher in this group compared to the other three groups. Moreover, inpatient days and clinic visits were higher and SMBG frequency was lower in this group compared to the other three groups. The present study revealed that inpatient days and clinic visits were positively correlated with physician-led insulin dose adjustment, and microvascular complications were positively correlated with insulin dose titration in the present study, which suggests that patients with long-term diabetes and diabetes-related microvascular complications focus more on glucose management for physicians and patients.

Lastly, 2542 (19.8%) of patients adopted combined physician and patient-led insulin titration (group D). Patients who received their first basal insulin treatment in an outpatient setting accounted for the highest proportion of patients in this group. Patients in this group

had the highest HbA1C level, glucose control level is a key factor for physician and patient to make insulin titration.

It is noteworthy that in the present study, HbA1C levels were reduced from 9.5% ± 2.0% to 7.4% ± 1.3%, with a mean reduction of 2.2% ± 2.0%. Overall, 41.7% of patients had HbA1C < 7%, of which 48.3%, 36.6%, 40.9%, and 38.8% of these patients were from group A,

Table III. *Dose titration model analysis in the past 6 months Multivariate-logistic (Reference group = No titration)*

Tabela III. *Wieloczynnikowa analiza regresji logistycznej modelu dostosowywania dawki w ciągu ostatnich 6 miesięcy (grupa odniesienia = brak dostosowywania dawki)*

Variables		OR(CI%)	P
Hospital level			
Tertiary Hospital vs. Secondary Hospital	Self-titration	0.904 (0.800, 1.021)	0.1041
Tertiary Hospital vs. Secondary Hospital	Physicians-led titration	0.901 (0.818, 0.993)	0.0359
Tertiary Hospital vs. Secondary Hospital	Cooperation-led titration	0.831 (0.739, 0.933)	0.0018
Age (years)	Self-titration	0.996 (0.989, 1.002)	0.2009
	Physicians-led titration	0.997 (0.992, 1.002)	0.2867
	Cooperation-led titration	0.986 (0.980, 0.993)	< 0.0001
BMI (kg/m²)	Self-titration	1.023 (1.005, 1.041)	0.0123
	Physicians-led titration	1.008 (0.994, 1.022)	0.2626
	Cooperation-led titration	1.025 (1.008, 1.042)	0.0035
Education degree	Self-titration	1.067 (1.008, 1.129)	0.0243
	Physicians-led titration	0.950 (0.908, 0.995)	0.0291
	Cooperation-led titration	0.941 (0.890, 0.994)	0.0290
Patient resource			
In-patient ward Vs Out-patient clinic	Self-titration	1.361 (1.203, 1.540)	< 0.0001
In-patient ward Vs Out-patient clinic	Physicians-led titration	2.771 (2.514, 3.055)	< 0.0001
In-patient ward Vs Out-patient clinic	Cooperation-led titration	3.026 (2.695, 3.397)	< 0.0001
Diabetes duration (year)	Self-titration	1.022 (1.010, 1.034)	0.0004
	Physicians-led titration	1.012 (1.002, 1.021)	0.0175
	Cooperation-led titration	1.017 (1.005, 1.029)	0.0038
Macro complication			
Yes vs. No	Self-titration	0.989 (0.840, 1.165)	0.8975
Yes vs. No	Physicians-led titration	1.081 (0.947, 1.235)	0.2496
Yes vs. No	Cooperation-led titration	1.250 (1.071, 1.459)	0.0046
Micro complication			
Yes vs. No	Self-titration	1.272 (1.118, 1.448)	0.0003
Yes vs. No	Physicians-led titration	1.014 (0.911, 1.127)	0.8043
Yes vs. No	Cooperation-led titration	1.230 (1.085, 1.395)	0.0012
HbA1c at V1 (%)	Self-titration	1.079 (1.047, 1.113)	< 0.0001
	Physicians-led titration	1.095 (1.068, 1.122)	< 0.0001
	Cooperation-led titration	1.139 (1.107, 1.173)	< 0.0001
Home blood glucose monitor			
Yes vs. No	Self-titration	1.640 (1.428, 1.884)	< 0.0001
Yes vs. No	Physicians-led titration	1.064 (0.955, 1.184)	0.2600
Yes vs. No	Cooperation-led titration	1.983 (1.735, 2.266)	< 0.0001
SMBG times	Self-titration	1.011 (1.002, 1.020)	0.0137
	Physicians-led titration	1.026 (1.018, 1.033)	< 0.0001
	Cooperation-led titration	1.029 (1.020, 1.037)	< 0.0001
Encouraged self-titration			
Yes vs. No	Self-titration	1.695 (1.505, 1.909)	< 0.0001
Yes vs. No	Physicians-led titration	0.927 (0.839, 1.023)	0.1321
Yes vs. No	Cooperation-led titration	2.140 (1.911, 2.396)	< 0.0001
Hospitalized			
Yes vs. No	Self-titration	0.831 (0.624, 1.107)	0.2059
Yes vs. No	Physicians-led titration	1.386 (1.124, 1.708)	0.0023
Yes vs. No	Cooperation-led titration	1.420 (1.112, 1.812)	0.0049
Out-patient clinic			
Yes vs. No	Self-titration	0.814 (0.688, 0.962)	0.0161
Yes vs. No	Physicians-led titration	2.440 (2.064, 2.884)	< 0.0001
Yes vs. No	Cooperation-led titration	2.148 (1.746, 2.643)	< 0.0001

BMI, body mass index; CI, confidence interval; HbA1C, glycated haemoglobin; OR, odds ratio; SMBG, self-monitoring of blood glucose

B, C, and D, respectively. A survey conducted in China [11] revealed that 34% of Chinese T2DM patients are treated with insulin. However, only 27% of these patients achieved the standard HbA1C of < 7%, with a mean disease duration of 3.7 years. In the present study, the average disease duration of patients was 6.5, 7.1, 6.8, and 6.9 years in group A, B, C, and D, respectively. One of the possible reasons for not achieving the standard HbA1C level was that patients started receiving insulin treatment a little late. Although the compliance rate of HbA1C was low, 24.8% of these patients did not adjust their insulin dose, and 15.3% of patients performed self-titration after six months of treatment in our study. The self-management of patients is essential for diabetes treatment and is highly recommended by guidelines worldwide. However, in real-world settings, the proportion of patients who did not adjust their insulin dose was high and the proportion of self-titration was low. Our study showed that fewer patients were encouraged to perform self-titration in the no-insulin-titration group. In clinical practice, physicians are required to fully understand the situation of patients receiving insulin for the first time and provide psychological counselling when necessary. This would help reduce the psychological burden of insulin treatment. In addition, physicians should encourage and instruct patients to adjust their insulin dose on their own to achieve better glycaemic control. The guidelines also recommend that, following the initiation of insulin therapy, physicians should positively encourage their patients to adjust their insulin dose, and should provide psychological counselling in order to encourage and teach patients to self-adjust their insulin dose.

Furthermore, the present study also revealed that patients who owned a glucometer were more likely to perform insulin dose adjustment. SMBG performance and higher frequency of SMBG had a positive effect on insulin dose adjustment in the present study. Some studies [13, 19, 20] have assessed the effect of SMBG control on HbA1C in type-1 and type-2 diabetes patients. The American Diabetes Association and Chinese guidelines for diabetes self-management recommend SMBG as an important tool in diabetes self-management. In the present study, 42.3%, 47.5%, 43.3%, and 49.3% of patients in group A, B, C, and D, respectively, owned a glucometer, and the frequency of SMBG in these groups was 5.3, 5.8, 5.0, and 5.3 times/month, respectively. After six months of follow-up, the percentage of patients who owned a glucometer in each of the four groups increased to 59.3%, 71.8%, 61.8%, and 74.8%, respectively, and the average frequency of SMBG increased to 5.5, 6.6, 6.5, and 7.5 times/month, respectively. Nonetheless, both factors were at a markedly low level. In China, glucometers and glucose test strips are not included in the medical insurance system, which may be the reason for the low level of SMBG in this population. This suggests that it is necessary to enhance the education of patients and improve national medical system policies as a way to encourage patients to conduct SMBG. Such measures would also help in insulin dose adjustment and increase compliance to target HbA1C levels.

To the best of our knowledge, this study is the first to evaluate the present situation of insulin titration in real-world clinical settings in China. More importantly, this is the first study that employed a large sample size comparing different insulin adjustments and investigate the factors that affect insulin adjustment in real-world settings. In this large observational study, patients with self-adjustment of insulin dose, physician-led insulin dose adjustment, and combined physician and patient-led adjustment experienced a reduction in their HbA1C levels. The HbA1C achievement rate was similar across the three groups (groups B, C, and D), with a considerably low incidence of severe hyperglycaemia events. Physician-led insulin dose adjustment accounted for 40–50% of the overall dose adjustment. However, self-led adjustment was associated with fewer clinic visits and lower costs. The effectiveness and safety of long-acting insulin over basal insulin therapy have been confirmed through a large number of randomised, controlled clinical studies. In the present study, the rate of hyperglycaemia events was similar and low in all four groups, suggesting that patients initiating basal insulin therapy can be encouraged to adjust their insulin dose on their own.

The present study has some limitations. First, this was an observational study, and the patient's treatment and follow-up were based on the physician's decision and the patient's willingness, which differs from the design of a randomised, controlled clinical study. Second, because the enrolled patients did not fully complete the required visits, no visits for laboratory tests were conducted, and patient data were only collected from patient information forms, there is a possibility of bias. In addition, some data were self-reported by patients, such as the frequency of hypoglycaemia and SMBG, which may not be accurate. Despite these limitations, the large sample size of the study is highly representative of the dose adjustment patterns in real-life clinical practice, with a preliminary exploration of factors that affect insulin treatment.

Conclusions

The present study is the largest in China to evaluate the factors that impact type 2 patients insulin dose adjustment while initiating basal insulin treatment in real-world clinical settings. It may help to find some problems and barriers in the initiation and titration of basal insulin. High HbA1C level, SMBG, long disease duration, microvascular complications, and the encouragement of physicians prompt patients to perform dose adjustments.

Implications/relevance for diabetes educators

Our study shows that encouragement from physicians is positively related with insulin self-adjustment. The findings suggest that when a patient starts to use insulin treatment, encouragement from physician is a key factor to seek insulin adjustment. Therefore, in real-world clinical settings, diabetes educators should encourage patients to adjust their insulin dose on their own. This is helpful for patients to achieve better glucose control.

Appendix

Members of the ORBIT Study Steering Committee are Linong Ji, Puhong Zhang, Jianping Weng, Juming Lu, Xiaohui Guo, Weiping Jia, Wenying Yang, Dajin Zou, Zhiguang Zhou, Changyu Pan, Yan Gao, Yangfeng Wu, and Satish K. Garg.

Acknowledgments

Author Contributions: Jing Chen contributed to the data analysis, interpretation of findings, and drafting of the manuscript. Jing Chen and Yingli Chen contributed to the study design, conduct, and data interpretation. Jing Chen and Linong Ji contributed to the study design and site selection. Puhong Zhang, Dongshan Zhu, Xian Li, and Jiachao Ji contributed to data analysis and interpretation of findings. Dongshan Zhu, Fang Zhao, and Heng Zhang contributed to suggestion and coordination for data analysis and manuscript drafting. The authors would like to thank the many investigators and patients for their participation, without which this study would not have been possible.

Funding support

This study was funded by Sanofi-Aventis (Shanghai, China). The funder did not participate in study design or execution, drug choice, data analysis, and reporting. The study was designed, executed, and analysed at the George Institute for Global Health at Peking University Health Science Centre.

Conflicts of interest

All authors have contributed significantly to the manuscript and declare that the work is original and has not been submitted or published elsewhere. None of the authors have any financial disclosure or conflict of interest.

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