

# Predictor variables and an equation for estimating HbA1c attainable by initiation of basal supported oral therapy†

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## ABSTRACT

**Aims/Introduction:** A method of estimating HbA1c attained after initiation of basal supported oral therapy (BOT) has not been reported previously. The aim of the present study was to determine which characteristics of patients could influence the effectiveness of BOT introduction, and to obtain an equation to estimate HbA1c after BOT initiation.

**Materials and Methods:** Sixty consecutive insulin-naïve type 2 diabetic patients with poor glycemic control (HbA1c  $\geq 7.5\%$ ) started once-daily injections of insulin glargine. Simple correlations were calculated between parameters such as HbA1c at baseline, HbA1c at week 24, reduction rate of HbA1c over 24 weeks (calculated as: [HbA1c level at baseline – HbA1c level at week 24]/HbA1c level at baseline), duration of diabetes, and the number of classes of coadministered oral antidiabetic drugs. Using multiple linear regression models, the independent effects of these parameters on HbA1c at week 24 were evaluated separately.

**Results:** Multiple linear regression analysis revealed that duration of diabetes ( $\beta = 0.561$ ;  $P < 0.001$ ) and HbA1c at baseline ( $\beta = 0.284$ ;  $P = 0.006$ ) were significant predictors of HbA1c at week 24. The best fitting multiple regression equation was: HbA1c at week 24 =  $0.078 \times$  duration of diabetes +  $0.218 \times$  HbA1c at baseline + 4.628 ( $r^2 = 0.437$ ).

**Conclusions:** The equation based on the multiple linear regression models indicates necessary conditions for type 2 diabetic patients to achieve target HbA1c. The present findings emphasize the principle that early initiation of BOT in type 2 diabetes effectively achieves good glycemic control. (*J Diabetes Invest*, doi: 10.1111/j.2040-1124.2011.00164.x, 2012)

**KEY WORDS:** Basal supported oral therapy, Insulin glargine, Insulin initiation

## INTRODUCTION

Since long-acting insulin analogs such as insulin glargine and insulin detemir<sup>1,2</sup>, as well as easy-to-use injection devices<sup>3</sup>, have been introduced, a variety of insulin treatment regimens have become available<sup>4</sup>, including basal supported oral therapy (BOT), which is combination treatment with oral antidiabetic drugs (OADs) and once-daily injection of a long-acting insulin analog. In addition to a substantial blood glucose-lowering action by insulin, BOT removes time-of-day constraints for insulin injection. It is also advantageous in that it facilitates the preparation of patients for insulin injections compared with intensive insulin therapy or multiple injections of premixed insulin formulas. In the consensus algorithm of the American Diabetes Association (ADA) and the European Association for the Study of Diabetes, BOT is recommended as the first choice for insulin therapy initiation<sup>5,6</sup>. There have been many reports regarding the efficacy of BOT introduction

for type 2 diabetic patients insufficiently controlled by OADs<sup>7–9</sup>. Several international trials have proved that HbA1c levels  $< 7.0\%$  are the most widely accepted target for glycemic control to prevent the complications of diabetes<sup>10–12</sup>. In the ADA treatment guidelines, lowering HbA1c  $< 7.0\%$  is also recommended to reduce microvascular and neuropathic complications of diabetes<sup>13</sup>.

Following the introduction of BOT, some patients reach HbA1c levels  $< 7.0\%$ . However, it remains to be determined which patient characteristics need to be checked to improve glycemic control as efficiently as possible with BOT. Therefore, the aim of the present study was to determine which patient characteristics influenced the effectiveness of BOT. There are few reports regarding estimates of achievable HbA1c levels following initiation of BOT. In the present study, we also aimed to obtain an equation to estimate HbA1c levels after BOT initiation. Patients with type 2 diabetes who started their first insulin therapy with BOT were reviewed with regard to several aspects, such as the number of coadministered OAD classes, the duration of diabetes, insulin dose, body mass index (BMI), and changes in HbA1c levels.

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## MATERIALS AND METHODS

### Patients

The subjects of the present study were 60 consecutive insulin-naïve type 2 diabetic patients who attended Tenri Hospital between 1 May 2005 and 30 April 2010 and who started once-daily injections of insulin glargine at bedtime or before breakfast. Insulin glargine was introduced to patients with poor glycemic control (i.e. HbA1c in the range 7.5–14.5%), on a diet with or without OADs and who provided informed consent to the therapy. They had taken up to three kinds of OADs (sulfonylureas, metformin,  $\alpha$ -glucosidase inhibitors, pioglitazone, and phenylalanine derivatives). The doses of OADs had not been changed for at least 1 month before the introduction of insulin. It was recommended that diet and physical activity remain stable during the study period. No other instructions or lifestyle advice were given. Exclusion criteria were previous or current treatments with insulin, clinically significant renal or hepatic disease, severe anemia, and current or clinical history of major psychiatric illness. The patients were divided into four groups according to the number of OADs used concomitantly at the time of BOT initiation: (i) no OAD (Group 0); (ii) one kind of OAD (Group 1); (iii) two kinds of OADs (Group 2); and (iv) three kinds of OADs (Group 3). Reductions in the number of classes and the dose of coadministered OADs were permitted when hypoglycemic episodes were suspected or reported for patients.

### Insulin Glargine Titration

The starting dose of insulin glargine (Lantus; Sanofi-Aventis, Paris, France) was set at 4–10 IU. Patients were asked to perform at least one measurement of capillary blood glucose before breakfast every day. The fasting blood glucose (FBG) target was 80–110 mg/dL (4.4–6.1 mmol/L). Using the glucose readings, patients were suggested to change insulin doses at every visit and followed continuously over 24 weeks.

### Outcome Measures

HbA1c levels, insulin glargine doses, body weight, and BMI were evaluated at baseline and at 12 and 24 weeks after insulin administration. The changes in HbA1c levels, body weight, and insulin dose were compared among the four groups. In the present study, according to the definition of the Japan Diabetes Society (JDS)<sup>14</sup>, the value for HbA1c (%) was estimated as an NGSP equivalent value (%) calculated using the formula  $\text{HbA1c (NGSP) (\%)} = \text{HbA1c (JDS) (\%)} + 0.4\%$ .

### Statistical Analysis

Data in the text and tables are given as the mean  $\pm$  SD. Simple correlations were calculated between parameters such as HbA1c level at baseline, HbA1c level at 24 weeks of treatment, reduction rate of HbA1c level over 24 weeks, duration of diabetes, and the number of classes of coadministered OADs. The reduction rate of HbA1c levels was calculated as:  $(\text{HbA1c level at baseline} - \text{HbA1c level at week 24})/\text{HbA1c level at baseline}$ .

Relationships between two variables (i.e. HbA1c level at baseline, HbA1c level at week 24, reduction rate of HbA1c level over 24 weeks, or duration of diabetes) were examined by two-tailed Pearson's correlation. The relationship between the number of classes of coadministered OADs and other variables (i.e. HbA1c level at baseline, HbA1c level at 24 weeks of treatment, reduction rate of HbA1c level over 24 weeks, and duration of diabetes) was examined by two-tailed Spearman's correlation.

Using a multiple linear regression model, the independent effects of these parameters on HbA1c level at week 24 were evaluated separately. Data were analyzed by analysis of variance followed by the Bonferroni–Dunn multiple comparison test. The Mann–Whitney *U*-test was used to compare parameters between men and women. In addition, the Mann–Whitney *U*-test was used to compare parameters between the group for whom OADs were decreased and the group without such a decrease, as well as between the group for whom doses of sulfonylureas were decreased and the group without such a decrease. The Chi-squared test of association was used to compare proportions across groups. Analyses were performed using SPSS version 15.0 (SPSS, Chicago, IL, USA).  $P < 0.05$  was considered significant.

## RESULTS

At BOT initiation, 10 patients had used no type of OAD, 19 patients had used one kind of OAD, 20 patients had used two kinds of OADs, and 11 patients had used three kinds of OADs, which formed the basis for the four separate groups for comparisons. Concomitantly used OADs at BOT initiation are given in Table 1. Most of the patients were administered sulfonylureas. Coadministered OADs such as  $\alpha$ -glucosidase inhibitors, pioglitazone, and phenylalanine derivatives had been taken for more than 3 months before insulin initiation. Forty-seven patients initiated insulin therapy after being administered sulfonylureas, metformin,  $\alpha$ -glucosidase inhibitors, pioglitazone, and phenylalanine derivatives for more than 3 months. Only one of 17 patients coadministered metformin and two of 49 patients

**Table 1** | Concomitantly used oral antidiabetic drugs at initiation of basal supported oral therapy

Concomitant OAD	<i>n</i>
SU	18
Glinide	1
SU + Met	9
SU + $\alpha$ GI	7
SU + TZD	4
SU + Met + $\alpha$ GI	7
SU + Met + TZD	1
SU + TZD + $\alpha$ GI	3

SU, sulfonylureas; Met, metformin; TZD, thiazolidinedione;  $\alpha$ GI,  $\alpha$ -glucosidase inhibitors; Glinide, phenylalanine derivatives; OAD, oral antidiabetic drug.

**Table 2** | Baseline characteristics of patients

	Group 0 (n = 10)	Group 1 (n = 19)	Group 2 (n = 20)	Group 3 (n = 11)	All patients (n = 60)	P value
Age (years)	60.2 ± 10.3	67.0 ± 9.5	64.5 ± 12.3	57.8 ± 11.0	63.4 ± 11.2	0.430
Male (%)	50.0	63.2	55.0	63.6	58.3	0.876
Duration of diabetes (years)	3.9 ± 3.6	10.6 ± 7.6	15.8 ± 7.3	17.5 ± 5.1	12.5 ± 7.9	<0.001
HbA1c (%)	10.1 ± 1.6	9.4 ± 1.1	9.7 ± 1.5	9.9 ± 1.8	9.7 ± 1.4	0.580
Insulin doses (IU)	9.0 ± 7.0	8.0 ± 4.6	6.6 ± 1.9	7.9 ± 5.3	7.7 ± 4.5	0.054
BMI (kg/m <sup>2</sup> )	23.7 ± 3.9	23.1 ± 2.8	24.7 ± 4.4	28.1 ± 5.1	24.7 ± 4.3	0.018
Weight (kg)	61.9 ± 11.3	61.1 ± 9.8	62.6 ± 12.3	76.1 ± 18.8	64.6 ± 13.8	0.019

BMI, body mass index. Unless indicated otherwise, data are the mean ± SD. All *P* values were determined by analysis of variance (for continuous variables) or Chi-squared tests (for gender comparison).

coadministered sulfonylureas had taken the OAD for 1 month before insulin initiation. Baseline clinical characteristics are summarized in Table 2. There were no significant differences between men and women in terms of HbA1c level at baseline, duration of diabetes, and BMI, or in changes in insulin dose, body weight, and HbA1c level (data not shown). At week 24, the number of classes of OADs was decreased in nine patients. Doses of sulfonylureas were reduced in 16 patients. There were no significant differences in changes in HbA1c (*P* = 0.65) or HbA1c at week 24 (*P* = 0.77) between the group for whom OADs were decreased and the group without such a decrease. There were also no significant differences in changes in HbA1c (*P* = 0.20) and HbA1c at week 24 (*P* = 0.85) between the group for whom doses of sulfonylureas were decreased and the group without such a reduction.

### Comparisons Among the Four Groups

There were no significant differences in HbA1c level at baseline among the four groups. Changes from baseline are summarized in Table 3. The average HbA1c level of 60 patients decreased from 9.7 ± 1.4% to 7.7 ± 1.1% over the 24-week treatment period following the start of insulin therapy. The proportion of patients who achieved an HbA1c level <7.0% at 24 weeks in Groups 0, 1, 2, and 3 was 60, 47, 15, and 0%, respectively. The more coadministered OADs patients had taken, the lower the

reduction rate of HbA1c level obtained (*P* = 0.001). There were significant differences in the duration of diabetes among the four groups (*P* < 0.001). Multiple comparison tests showed significant differences among the four groups, except between Groups 2 and 3 (*P* = 0.491). There were no significant differences in HbA1c levels at baseline (*P* = 0.580) among the four groups, but there were significant differences in HbA1c level at 24 weeks (*P* = 0.015). There were no significant differences in either insulin dose at the start of BOT (*P* = 0.054) or during treatment (*P* = 0.084) among the four groups. BMI was significantly higher in Group 3 than in the other groups at the start of BOT (*P* = 0.018). However, in terms of changes in body weight, there were no significant differences between the four groups (*P* = 0.234).

### Correlations Among Variables

The number of classes of coadministered OADs was positively correlated with the duration of diabetes (*P* < 0.001) and negatively correlated with the reduction rate of HbA1c level (*P* = 0.001; Table 4). The reduction rate of HbA1c level was negatively correlated with the duration of diabetes (*P* = 0.001). The HbA1c level at 24 weeks of treatment was significantly correlated with the duration of diabetes (*P* < 0.001), the reduction rate of HbA1c level (*P* < 0.001), and the number of classes of coadministered OADs (*P* < 0.001). The HbA1c level at 24 weeks of treatment was

**Table 3** | Changes from baseline to week 24

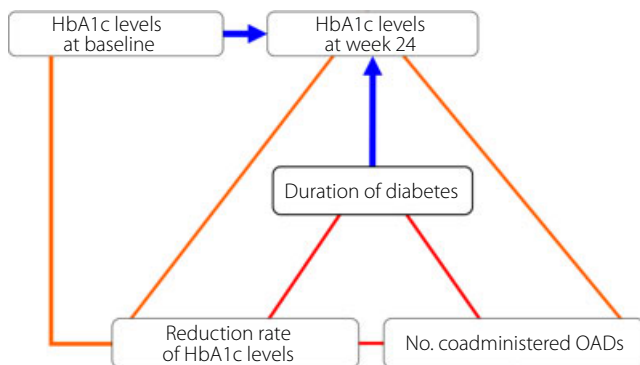
	Group 0 (n = 10)	Group 1 (n = 19)	Group 2 (n = 20)	Group 3 (n = 11)	All patients (n = 60)	P value
HbA1c at week 12 (%)	7.6 ± 0.8	7.4 ± 1.1	8.0 ± 0.9	8.4 ± 1.0	7.8 ± 1.0	0.071
HbA1c at week 24 (%)	7.1 ± 0.6	7.4 ± 1.2	7.8 ± 0.6	8.7 ± 1.2	7.7 ± 1.1	0.015
Change from baseline to week 24 (%)	3.0 ± 1.5	2.0 ± 1.6	2.0 ± 1.4	1.2 ± 0.9	2.0 ± 1.5	0.041
Reduction rate of HbA1c (%)	28.8 ± 10.5	20.4 ± 14.4	18.8 ± 10.3	11.8 ± 7.5	19.7 ± 12.2	0.012
Insulin doses at week 12 (IU)	11.5 ± 8.9	9.1 ± 4.1	7.2 ± 2.0	11.2 ± 6.1	9.2 ± 5.3	0.087
Insulin doses at week 24 (IU)	10.7 ± 9.3	9.5 ± 4.2	7.4 ± 1.8	12.2 ± 5.8	9.5 ± 5.3	0.084
Change from baseline to week 24 (IU)	1.7 ± 3.1	1.5 ± 4.9	0.8 ± 1.5	4.3 ± 2.6	1.8 ± 3.5	0.057
Weight at week 12 (kg)	61.7 ± 12.7	60.6 ± 9.9	62.5 ± 11.2	76.9 ± 18.9	64.5 ± 13.9	0.009
Weight at week 24 (kg)	60.4 ± 10.3	60.8 ± 10.3	62.9 ± 11.2	77.1 ± 19.4	64.6 ± 14.2	0.009
Change from baseline to week 24 (kg)	-1.5 ± 3.5	-0.3 ± 2.9	0.3 ± 2.5	1.0 ± 2.7	0.0 ± 2.9	0.234

Unless indicated otherwise, data are the mean ± SD. All *P* values were determined by analysis of variance.

**Table 4** | Correlations between variables

N = 60	Concomitant OADs	Reduction rate of HbA1c levels	HbA1c at baseline	HbA1c at week 24
Duration of diabetes	$r = 0.620, P < 0.001$	$r = -0.423, P = 0.001$	$r = 0.131, P = 0.318$	$r = 0.598, P < 0.001$
Concomitant OADs	–	$r = -0.414, P = 0.001$	$r = -0.017, P = 0.899$	$r = 0.496, P < 0.001$
Reduction rate of HbA1c	–	–	$r = 0.566, P < 0.001$	$r = -0.558, P < 0.001$
HbA1c at baseline	–	–	–	$r = 0.357, P = 0.005$

The reduction rate of HbA1c was calculated as: (HbA1c level at baseline – HbA1c level at week 24)/HbA1c level at baseline. The correlation between any of the two continuous variables was examined by the two-tailed Pearson's method. The correlation between a discrete variable, such as the number of classes of oral antidiabetic drugs (OADs), and continuous variables was examined using the two-tailed Spearman's method. Concomitant OADs, concomitant oral antidiabetic drugs at initiation of basal supported oral therapy.



**Figure 1** | Duration of diabetes and HbA1c levels at baseline were significant determinants of the HbA1c level at 24 weeks. The HbA1c level to be attained at week 24 is calculated from the duration of diabetes and the HbA1c level at baseline.

also significantly correlated with the HbA1c level at baseline ( $P = 0.005$ ). The reduction rate of HbA1c level was positively correlated with HbA1c level at baseline ( $P < 0.001$ ).

### Multiple Regression Model

Multiple linear regression analysis including HbA1c level at baseline, duration of diabetes, the number of classes of coadministered OADs, and HbA1c level at week 24 revealed that the duration of diabetes ( $\beta = 0.561; P < 0.001$ ) and HbA1c level at baseline ( $\beta = 0.284; P = 0.006$ ) were significant determinants of HbA1c level at 24 weeks (Figure 1). The best fitting multiple regression equation was: HbA1c level at week 24 =  $0.078 \times$  duration of diabetes +  $0.218 \times$  HbA1c level at baseline + 4.628 ( $r = 0.661; r^2 = 0.437$ ), on the conditions of diabetic duration in the range 1–35 years and HbA1c level in the range 7.5–14.5%.

### DISCUSSION

The present study showed a significant HbA1c reduction by 2.0% in 6 months following BOT introduction from a mean HbA1c level of 9.7% at baseline. In the Treat to Target Trial<sup>15</sup> and the DURABLE trial<sup>16</sup>, long-acting insulin analogs added to oral therapy reduced HbA1c levels by 1.7% in 24 weeks. The LANMET study<sup>17</sup> showed that HbA1c was decreased by

2.0% in 36 weeks following BOT introduction. In the APOLLO study, the decrease in HbA1c was 1.7% in 44 weeks with BOT<sup>18</sup>. Rosenstock *et al.*<sup>19</sup> reported that insulin glargine initiation reduced HbA1c by 1.5% in 52 weeks. Mean HbA1c levels at baseline in these studies were reported to be 8.6–9.5%<sup>15–19</sup>, similar to those in the present study. Almost the same reduction in HbA1c levels from baseline to that found in the present study suggests that the addition of once-daily long-acting insulin to oral therapy is as effective for Japanese patients as for Western patients.

In the Treat to Target Trial<sup>15</sup>, the average insulin dose at 24 weeks was 47.2 IU and BMI was 32.5 kg/m<sup>2</sup>. In the DURABLE trial<sup>16</sup>, the average insulin dose at week 24 was 35 IU and BMI was 32 kg/m<sup>2</sup>. In the present study, the average dose of insulin glargine at week 24 was 9.5 IU and BMI was 24.7 kg/m<sup>2</sup>. The insulin doses of patients in Groups 2 and 3, whose HbA1c levels remained above 7.5% at week 24, were 7.4 and 12.2 IU, respectively. Those in Groups 0 and 1, whose HbA1c levels were <7.5% at week 24, were 10.7 and 9.5 IU, respectively. Goto *et al.*<sup>20</sup> reported that, at 6 months, BMI was 24.4 kg/m<sup>2</sup> and the average dose of insulin glargine was 7.6 IU. Kawamori *et al.*<sup>21</sup> reported that the average dose of insulin glargine at week 28 was  $11.08 \pm 0.52$  IU. The insulin dose at week 24 in the present study was smaller than that in the aforementioned studies for Western patients. However, it was similar to that reported by other studies in Japanese people. In Groups 2 and 3, the dose of insulin could not be increased because of hypoglycemia. Some patients were not able to receive sufficiently increased doses of insulin to lower the average FBG below 110 mg/dL (6.1 mmol/L) because they occasionally experienced hypoglycemic events. Some patients were not able to achieve HbA1c <7.0%, even though their FBG was <110 mg/dL (6.1 mmol/L) because their postprandial glucose was so high. Goto *et al.*<sup>20</sup> reported that the average insulin dose of the improved group (HbA1c < 7.5%) was  $6.7 \pm 0.3$  IU, whereas that of the non-improved group (HbA1c  $\geq 7.5\%$ ) was  $8.2 \pm 1.0$  IU. This is similar to the results obtained in the present study. The difference in BMI and insulin sensitivity between Westerners and Japanese people may account for the differences in total doses of insulin glargine between other studies for Westerners and the present study.



Although mean HbA1c levels evidently improved on BOT initiation, a substantial proportion of patients could not reach the target level of HbA1c. Achievement rates of HbA1c <7.0% have been reported to be 40–65%<sup>15–19</sup>. In fact, some patients can achieve target glycemic control following BOT introduction, whereas some cannot. Multiple regression analysis was used in the present study to examine the clinical characteristics that affected the response to BOT initiation.

Multiple linear regression analysis using HbA1c level at baseline, duration of diabetes, number of classes of coadministered OADs, and HbA1c level at 24 weeks of BOT as variables revealed that the duration of diabetes and HbA1c level at baseline were significant predictors of the HbA1c level at 24 weeks of BOT. The best fitting multiple regression equation was HbA1c level at week 24 (%) =  $0.078 \times \text{duration of diabetes (years)} + 0.218 \times \text{HbA1c level at baseline (\%)} + 4.628$ . Using the multiple regression equation, we can estimate attainable HbA1c levels following BOT initiation from two readily available parameters. From the multiple regression analysis, when the target HbA1c level should be <7.0%, the condition that must be met was estimated as: HbA1c level on BOT initiation <  $(-0.358 \times \text{duration of diabetes [years]} + 10.88)$ . The multiple regression equation could be useful as a guide, in that the HbA1c level to be attained at week 24 is calculated from the duration of diabetes and the HbA1c level at baseline. This approach should be helpful for patients as well as for clinicians in deciding the mode of insulin treatment, including injection frequency. From the multiple regression equation, when the target HbA1c level is <7.0%, we have to initiate BOT with the following conditions: type 2 diabetic patients with HbA1c level  $\leq 8.0\%$  at baseline and duration of diabetes  $\leq 8$  years. By comparison, if the duration of diabetes is  $\leq 5$  years, BOT could be initiated when HbA1c levels are  $\leq 9.0\%$ , resulting in an HbA1c level at 24 weeks of <7.0%.

There are a few limitations to the present study. First, it was an observational study rather than a controlled study. Because it was not a prospectively designed study, there are some limits to interpreting the results. However, it is suggested that early initiation of BOT before a longer duration of diabetes and before adding a few more classes of OADs is efficacious in achieving optimal glycemic control. Second, the present findings cannot indicate what kinds of OADs are best partner to use with BOT, because the number of patients in the study was not large enough for this analysis. Third, the present results cannot show the efficacy of adding another OAD for type 2 diabetic patients who had initiated BOT. Despite these limitations, the present study is important in that HbA1c levels after BOT initiation can be estimated using the duration of diabetes and the HbA1c level at baseline, parameters that are easily determined in the clinical setting. A method of estimating HbA1c levels using such parameters has not been reported previously as far as we know.

The present findings indicate that combination of too many OADs and/or overlone duration of diabetes with insufficient glycemic control lead to belated BOT introduction with half the improvement in HbA1c level. Patients with type 2 diabetes on OAD monotherapy should switch to the next step, such as the

addition of a second OAD or the initiation of insulin injections, if there is insufficient glycemic control. In addition, when good glycemic control is not achieved on combination OAD therapy, a prompt change to insulin is desirable. Continuing combination OAD therapy with poor glycemic control should be avoided as much as possible. According to the stepwise therapy of type 2 diabetes given in treatment guidelines<sup>5,6</sup>, patients with poor glycemic control despite being on diet and exercise therapy should start OAD monotherapy. Sulfonylureas are often the first OAD chosen and administered in Japan, unlike in the US and Europe<sup>22</sup>. In addition, sulfonylureas are the OADs most frequently used concomitantly with basal insulin in Japan<sup>20,21</sup>. When optimal glycemic control is not achieved with OAD monotherapy, a second class of OAD could often be added to the first OAD. Then, sometimes, a third class of OAD may be added if good glycemic control is not attained. In the present study, the more OADs that patients were taking, the longer the duration of diabetes. However, the longer the duration of diabetes, the lower the decrease in HbA1c after BOT introduction. The addition of a second or a third OAD and continuing combination OAD therapy does not necessarily progress to the timely initiation of insulin therapy to achieve good glycemic control. It has been reported that the longer the duration of diabetes, the less insulin secretion accrues<sup>23,24</sup>. The findings of the present study are consistent in that the more OADs that patients took concomitantly and the longer duration of diabetes, the less insulin secretion accrued.

Many patients and physicians are reluctant to begin insulin injections, which is common in the treatment of type 2 diabetes; this is called psychological insulin resistance<sup>25,26</sup>. Psychological insulin resistance delays the start of insulin therapy, and patients and physicians miss the chance to start insulin therapy at an appropriate time<sup>27</sup>. BOT could be the easiest and most effective choice for initiating insulin therapy in outpatient situations.

In conclusion, the equation based on the multiple linear regression model indicates easily determined conditions necessary for type 2 diabetic patients to achieve target HbA1c levels. The less the duration of diabetes, the greater the reduction in HbA1c levels obtained. Early initiation of BOT in type 2 diabetes, which is a pathophysiologically progressive disease, is very likely to be more effective in achieving good glycemic control. This information could be useful for patients, as well as clinicians, to lessen the barriers to starting once-daily insulin injections in the real world.

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