Analysis for the Improvement of Inadequate Glycemic Control in Patients with Type 2 Diabetes Mellitus in Nagano, Japan

Ai SATO[1)†], Yoshihiko SATO[1)*†], Yuki KOBAYASHI[1)]
Masanori YAMAZAKI[1)2)] and Mitsuhisa KOMATSU[1)]

1) *Division of Diabetes, Endocrinology and Metabolism, Department of Internal Medicine, Shinshu University School of Medicine*
2) *Department of Drug Discovery Science, Shinshu University School of Medicine*

Objectives and Methods : The present study was performed to determine whether patients with HbA1c ≥ 7.0 % can show improvement with additive treatments. A total of 252 patients ≤ 75 years old with type 2 diabetes mellitus (T2DM) and with HbA1c ≥ 7.0 % were enrolled in this study. The primary endpoint was a rate of achievement of HbA1c < 7.0 % in 1 year.

Results : HbA1c was ≥ 7.0 % (7.0 %–10.1 %) in all patients in the study population. Initially, mean HbA1c was 7.66 % ± 0.59 %. Thus, treatments were changed for 50.4 % of patients. However, treatment was not changed in nearly half of the patients. In 3 months, mean HbA1c remained at 7.63 % ± 0.83 %, and HbA1c was < 7.0 % in only 18.3 % of patients. At this time point, treatments were changed in 68.3 % of patients. Over 1 year, treatments were changed in a total of 86.5 % of the patients. However, only 27.8 % of patients had HbA1c < 7.0 % within 1 year.

Conclusion : The rate of reaching the target HbA1c in 1 year was only 27.8 % in our study population. This was not sufficient for the control of blood glucose (BG). Thus, greater treatment intensity and further planning to improve patient condition are required to achieve the target. *Shinshu Med J 66 : 319—324, 2018*

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Key words : type 2 diabetes mellitus, inadequate glycemic control, clinical inertia

I Introduction

Diabetes is a disease with a worldwide distribution, which causes microvascular and macrovascular complications. The aim of treatment of diabetic patients is to avoid these complications by controlling blood glucose (BG) and to maintain the quality of patients' lives. Hemoglobin A1c (HbA1c) is commonly used as a marker of daily glycemic control. In 2013, the Japan Diabetes Society (JDS) reported the target HbA1c level as < 7.0 %, which has been proven to be appropriate by many prospective studies performed around the world[1)-3)].

Approaches to control BG in type 2 diabetes mellitus (T2DM) include lifestyle improvements, such as diet and exercise. If these approaches are insufficient for the control of BG, several medications, such as oral hypoglycemic agents (OHA) or injection of glucagon-like peptide-1 receptor agonists (GLP-1RA) or insulin, are selected as additional treatments. However, more than half of all patients with T2DM in Japan do not reach the target level of HbA1c[4)].

Previously, we analyzed the level of BG control in diabetic patients treated in clinics or hospitals in Nagano prefecture (presented at the annual meeting of the JDS in 2013). In 2007, the mean HbA1c level of all enrolled patients was 7.29 %. In Japan, the Diabe-

* Corresponding author : Yoshihiko Sato
Division of Diabetes, Endocrinology and Metabolism, Department of Internal Medicine, Shinshu University School of Medicine, 3-1-1 Asahi, Matsumoto, Nagano 390-8621, Japan
E-mail : ysato@shinshu-u.ac.jp
† Ai Sato and Yoshihiko Sato equally contributed to this study

Table 1 Mean HbA1c levels of diabetic patients in 2007 and 2012 in Nagano, Japan

Year	2007	2012	*P*-value
n	3515	7418	
Sex			
Male	1920 (55.2)	4312 (58.4)	
Female	1558 (44.8)	3069 (41.6)	< 0.01
Age (years old)	66.3 ± 12.3	66.8 ± 12.4	0.07
Body mass index (kg/m^2)	24.3 ± 3.8	24.9 ± 5.3	< 0.01
HbA1c (%)	7.29 ± 1.18	7.19 ± 1.20	< 0.01
Number of drugs for diabetes	1.49 ± 0.94	1.68 ± 1.12	< 0.01
Blood pressure			
Systolic	132.8 ± 15.0	132.9 ± 18.8	0.84
Diastolic	76.0 ± 10.6	75.6 ± 10.7	0.10

Data are n (%) or mean ± SD.

tes Clinical Data Management Study Group (JDDM) began to collect annual data of mean HbA1c levels of diabetic patients in 2000[4], and our data were similar to those reported by the JDDM[5]. In 2012, however, although new treatment methods, such as DPP4 inhibitors and GLP-1RA had become available in 2009 and 2010, respectively[6,7], the mean HbA1c level had only decreased slightly to 7.19 % **(Table 1)**.

In this study, we examined whether patients with HbA1c ≥ 7.0 % can be improved with more stringent treatment, e.g., the addition of new drugs and intensification of dietary control and exercise.

Ⅱ Materials and Methods

A Ethics

The study protocol was approved by the ethics committee of Shinshu University School of Medicine (Approved number 2273). All patients provided informed consent before participation.

B Inclusion criteria

A total of 270 consecutive T2DM patients ≤ 75 years old (25–75 years old) with HbA1c ≥ 7.0 % (7.0–10.1 %) from three clinics and six hospitals during the period from 3 September 2013 to 13 February 2014 were included in the study. We collected clinical data as shown in **Fig. 1**. The primary endpoint was a rate of achievement of HbA1c < 7.0 % in 1 year. Medical staff, including doctors of internal medicine, nurses, nutritionists, pharmacists, and exercise trainers, tried to improve HbA1c to < 7.0 % within 1 year. There were no special rules regarding how to improve glycemic control, except for no changes in treatment within 3 months after an initial change. As we did not obtain data about HbA1c in 1 year from 18 patients, the data from 252 patients were included in the study.

C Statistical analysis

Values were compared using Welch's *t* test, or χ^2 test. In all analyses, $P < 0.05$ was taken to indicate statistical significance.

Ⅲ Results

The mean age, body mass index, and HbA1c level were 60.0 ± 10.3 years, 25.9 ± 4.4 kg/m^2, and 7.66 % ± 0.59 %, respectively, at the start of the study **(Table 2)**. HbA1c was ≥ 7.0 % in all patients (7.0 %–10.1 %). Treatments were changed in 50.4 % of patients at the start of the study. Specifically, 69 patients (27.4 %) changed or added a new medication, and 2 out of 69 patients changed their medication with intensification of diet and/or exercise. 58 patients (23.0 %) intensified their diet and/or exercise without changing medication. However, nearly half of the patients did not change their treatments at this point **(Fig. 2, Table 2)**. In 3 months, mean HbA1c remained at 7.63 % ± 0.83 %, and only 18.3 % of patients had HbA1c < 7.0 %. Here, 31.3 % of patients changed or added some treatments, so a total of 68.3 % changed their treatments during 0 and 3 months **(Fig. 2)**. Subsequently, 53.6 % of patients received a new treat-

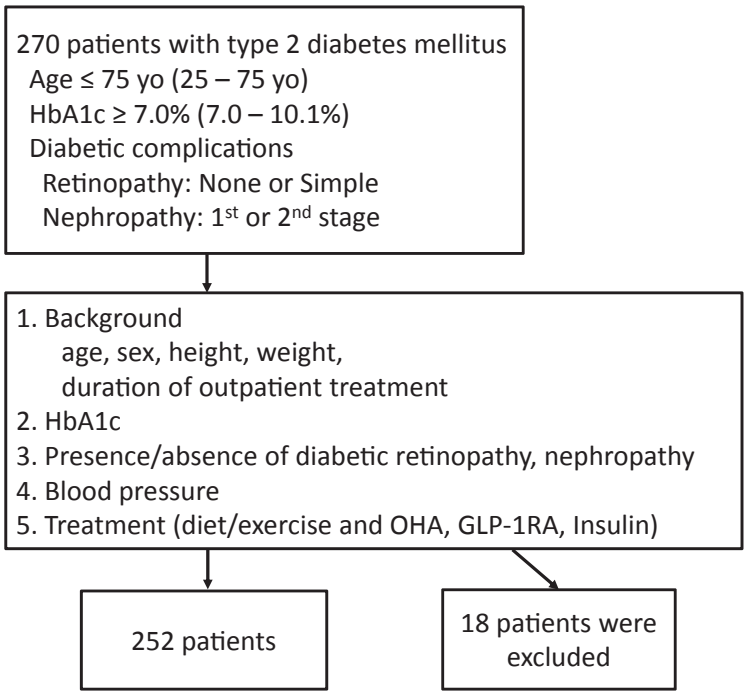

Fig. 1 Enrollment of patients.
A total of 270 diabetic patients were initially enrolled in the study. They were ≤ 75 years old and had HbA1c ≥ 7.0 %. We collected clinical data as outlined above. Finally, 252 patients were included in the study.

Table 2 Background of patients and initial changes of treatment at 0 months

n		252
Sex		
Male		149 (59.1)
Female		103 (40.9)
Age (years old)		60.0 ± 10.3
Body mass index (kg/m^2)		25.9 ± 4.4
HbA1c (%)		7.66 ± 0.59
Changes of treatment on enrollment	Medication + Diet/Exercise	2 (0.8)
	Medication only	67 (26.6)
	Diet/Exercise only	58 (23.0)
	No change of treatment	125 (49.6)

Data are n (%) or mean ± SD.

ment approach during the period from 3 to 12 months ; therefore, the treatment approach was changed in a total of 86.5 % of cases over the period of 12 months **(Fig. 2)**. However, mean HbA1c was 7.59 % ± 0.96 %, and only 27.8 % of patients had HbA1c < 7.0 % within 1 year **(Fig. 2, Table 3)**. Changes in both medication and diet/exercise showed a better tendency on the rate of HbA1c improvement compared with no change of treatment, although there was no statistical significance **(Table 3)**.

Finally, we evaluated the relationship between initial HbA1c level and the rate of achievement of HbA1c < 7.0 % within 1 year. As expected, patients with initial HbA1c < 8.0 % showed better improvement than those with HbA1c ≥ 8.0 %. None of the patients with initial HbA1c ≥ 9.0 % reached HbA1c < 7.0 % within 1 year **(Table 4)**.

Ⅳ Discussion

Despite the development of several new treatments for T2DM, nearly half of the patients did not show sufficient daily BG control[5]. The reasons may vary, e.g., problems in daily life, such as overeating or lack of exercise, or medications may not be sufficiently efficacious in some patients. In daily medical treatment, it is necessary to identify the specific

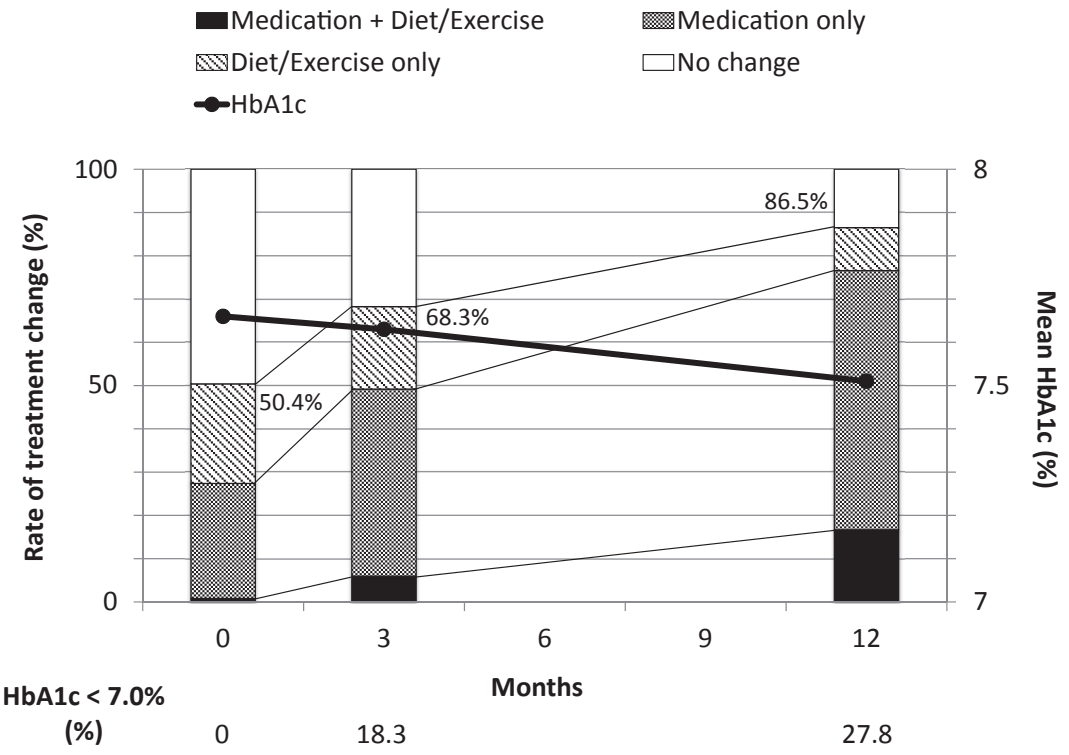

Fig. 2 Rates of treatment change and mean HbA1c at 0, 3, and 12 months.
The total rate of change in medication and diet/exercise for improvement of BG increased gradually.
The mean HbA1c was 7.66 % ± 0.59 %, 7.63 % ± 0.83 %, and 7.51 % ± 0.96 % at 0, 3, and 12 months, respectively.

Table 3 Relationship between change of treatment and rate of patients who achieved HbA1c < 7.0 % in 1 year

Changes of treatment	No. of patients	Patients with HbA1c < 7.0 %	*P*-value
All patients	252	70 (27.8)	-
Medication + Diet/Exercise	42 (16.7)	14 (33.3)	0.22
Medication only	151 (60.0)	42 (27.8)	0.39
Diet/Exercise only	25 (9.9)	7 (28.0)	0.50
No change of treatment	34 (13.5)	7 (20.6)	-

Data are n (%). *P*-values are for comparison with no change of treatment.

Table 4 Relationship between initial HbA1c level and rate of patients who achieved HbA1c < 7.0 % in 1 year

HbA1c (%) on enrollment	n	Change in HbA1c (%)	Achievement in 1 year	*P*-value
7.0 – 7.9	190 (75.4)	−0.08	62 (32.6)	-
8.0 – 8.9	51 (20.2)	−0.39	8 (15.7)	< 0.05
≥ 9.0	11 (4.4)	−0.04	0 (0.0)	< 0.05

Data are n (%). *P*-values are for comparisons of 7.0 % – 7.9 % to 8.0 % – 8.9 %, ≥ 9.0 %, respectively.

problems for each patient. However, this is sometimes difficult because of a lack of information regarding the daily lives of patients.

Seven types of OHA, GLP-1RA, and insulin are currently available for the treatment of T2DM. Many diabetic patients do not adhere to ideal diet

control or exercise in their daily lives, and therefore there are many approaches to improve BG.

In this study, we could have changed or intensified glycemic management because all patients had HbA1c ≥ 7.0 %. However, 13.5 % of patients did not receive new treatments during the test period despite the availability of multiple tools for glycemic control.

In daily outpatient clinics, clinicians tend to be slow to intensify glycemic control. This is so-called clinical inertia, defined as "recognizing the problem but failing to act"[8)-10)]. Strain et al. suggested that impairment of communication lies at the heart of clinical inertia[9)]. This is often the case in daily treatment of diabetes, and clinicians should not compromise the treatment for improvement of glycemic control.

In 2014, we obtained further unique tools for the treatment of T2DM, i.e., sodium-glucose co-transporter 2 inhibitor (SGLT2i). The major feature of this drug is excretion of a certain amount of glucose in the urine[11)12)], which enables decreases in not only BG but also body weight of patients. Thus, we can expect about 0.8 %-1.0 % reduction of HbA1c and 2-3 kg of body weight with SGLT2i. When this study began in 2013, SGLT2is were not in clinical use in Japan. These drugs became available in April 2014, so many clinicians seldom prescribed SGLT2is during the study period. Therefore, further studies are required to re-estimate the improvement of HbA1c with these drugs.

V Conclusions

The rate of reaching the target HbA1c < 7.0 % in 1 year was only 27.8 %. This rate was disappointing, and insufficient for the control of daily BG. To achieve the target, more intensive treatments and more precise analysis of problems specific for each patient are required. Then, we should plan how to improve the patients' condition and empower the patients themselves to control their disease.

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Disclosures

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The other authors have no potential conflicts of interest associated with this research.

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