【論　　文】

The Suppression of Seasonal Exacerbation in HbA1c in Mellitus Patients with Type 2 Diabetes in Japan

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【Abstract】

Type 2 diabetes mellitus patients show seasonal variation in their hemoglobin A 1 c levels. Seasonal variation in hemoglobin A 1 c levels was able to observe in type 2 diabetes mellitus patients; it decreased between summer and autumn and increased in winter to spring. HbA 1 c in diet-educated type 2 diabetic mellitus patients decreased independently of seasonal variation. Furthermore, early intervention improved blood glucose levels effectively; this may prove to be important in regulating carbohydrate metabolism in type 2 diabetes mellitus patients who receive dietary education.

【Keywords】

Dietary education　Type 2 diabetes mellitus　HbA 1 c
Retrospective observational study

INTRODUCTION

The treatment of type 2 diabetes mellitus includes preventing lifestyle-related diseases by managing weight, blood glucose and serum lipid levels, and blood pressure; the aim is to inhibit the onset and development of additional serious illness. The treatment strategy for a patient's lifestyle is aimed at correcting eating behaviors, losing weight, and administering oral medicine[1-3]. Furthermore, appropriate choices of diet and exercise therapy and pharmacotherapy are important to the patient's lifestyle and activities of daily living[4]. On the other hand, blood glucose levels of the type 2 diabetes mellitus patient change seasonally, and lifestyle education and therapeutic reinforcement that consider this seasonal periodicity are required[5, 6]. However, dynamic changes in seasonal periodicity of the blood glucose levels by dietary education (DE) intervention have rarely been studied. Here we analyzed time series changes in hemoglobin A 1 c (HbA 1 c) levels of type 2 diabetes mellitus patients and investigated the influence of DE on the seasonal periodicity of HbA 1 c.

MATERIALS AND METHODS

Patients

This is a retrospective observational study of 131 type 2 diabetes mellitus outpatients at Inobe Hospital with whose HbA1c levels were≥6.5%, conducted from January 1, 2012, to December 31, 2014. Patients who had insulin therapy and any change of type 2 diabetes mellitus medication were not included. Because the Ethics Committee of Inobe Hospital waived the necessity of approving the study, we registered it online in the University Hospital's Medical Information Network (No. 000014977).

The DE intervention was used for 37 patients (DE group), and the nonintervention [usual care (UC)] group contained 94 patients. Table 1 shows clinical features of the study participants at baseline. The baseline study period was defined as medical consultation during April 2012. Follow-up assessments were conducted annually each April. Furthermore, this study divided the four phases of spring, summer, autumn and winter in view of the characteristics of seasonal variation in Japan[7]. Since the study is a retrospective observational study, the patient's background, the disease period, the complications, the type and dose of oral hypoglycemic medications, and the history of dietary education were not considered. But patients using insulin preparations were excluded from this study.

DE

A DE intervention was designed for those patients whose doctors judged that improvement in their eating habits were necessary. In addition, patients who consented to receive treatment to improve their diet were defined as the DE group. Four periods for this DE intervention were designated as follows: phase 1 [April to June (N=10)], phase 2 [July to September (N=13)]; phase 3 [October to December (N=7)], and phase 4 [January to March (N=7)]. At the patients' monthly medical consultation, we performed an individual DE intervention of approximately 15 min. The DE contents were based on the living condition of a particular patient. Using a behavior modification theory[8, 9] and diabetes mellitus treatment guideline[10],we set energy intake at 25–35 kcal/standard weight (kg)[10]. First, we understood the patient's lifestyle situation and taste preferences. Then, we performed DE using the food exchange lists method[11], charting of the body weight[12], and training in food selection[13].

Charting of daily weight pattern

The charting enables objective visual depiction of body weight and eating behaviors of the patients to support weight loss[14]. The patient recorded measurements four times every day: "just after waking up", "just after breakfast", "just after dinner", and "just before going to bed"[12, 15]. This study required patients to chart their data during the entire DE intervention period.

Food selection training

This study performed food selection training in the DE intervention once a month. This is a virtual method to evaluate eating behavior using food cards[16]. We calculated nutrients and calories in the ingredients of the foods that patients selected. They compared the nutrient values of their chosen foods and made voluntary choices. Food selection training was incorporated into the treatment program as a method to promote transformation of the eating behavior of the patient voluntarily[13].

Clinical examination

Laboratory tests were performed at each medical consultation, and HbA 1 c (%) was assayed by the latex agglomeration turbidimetric method of Bio Majesty 9030 (JEOL, Ltd., Tokyo, Japan) in accordance with the National Glycohemoglobin Standardization Program (NGSP)[17]. We measured the height and weight of each patient each time to calculate body mass index (BMI, kg/m^2).

Endpoint

Monthly HbA 1 c levels were compared with the baseline levels. Furthermore, we compared HbA 1 c levels every month for the DE and UC groups. We monitored HbA 1 c levels for 18 months from the initial DE for examining the correction effect on HbA 1 c levels.

Statistical analysis

Statistical evaluations were performed with JMP (version10. 0. 0, windows from SAS) software using, and all parameters were non-normal distribution compliant by the Shapiro-Wilk test. Continuous variables are presented as median and interquartile ranges (IQRs). Categorical variables are presented as numbers. Pearson's chi-square test was used for comparisons between sex. Mann-Whitney U test were used for comparisons analysis between groups. Wilcoxon signed-rank test was used to compare the variational parameters each group. Statistical significance was accepted at $P<0.05$.

Results

Clinical Characteristics of the Participants

All study population characteristics shown in Table 1 failed to conform to the normal distribution according to the Shapiro-Wilk normality test ($P<0.05$). The only statistically significant differences in baseline characteristics between the groups were mean age ($P=0.0171$), mean body weight ($P=0.0217$), and mean BMI ($P=0.0068$). The mean age was significantly lower in the DE group. In outcome, the mean BMI between the DE and UC groups were not significantly different ($P=0.3317$), which implies that HbA 1 c was significantly lower in the DE than in the UC group ($P=0.0007$, Table 2).

Table 1. Baseline characteristics of the type 2 diabetes mellitus patients

	UC Group		All DE Groups		*P*-value
N	94		37		
Sex (Male/Female)	43 / 51		12 / 25		0.1607
Age	69.5	[62.0 - 76.0]	62.0	[57.0 - 70.0]	0.0171
Height (cm)	155.5	[148.0 - 166.1]	154.7	[153.0 - 164.0]	0.8360
Body weight (kg)	59.2	[54.6 - 66.9]	70.8	[56.1 - 86.5]	0.0217
Body Mass Index (kg/m^2)	24.8	[23.3 - 26.2]	26.6	[24.0 - 32.8]	0.0068
HbA1c (%)	6.8	[6.6 - 7.2]	6.8	[6.1 - 8.0]	0.6862

For number of patients (N) and sex (Male / Female), the table gives frequencies; other numbers represent medians [IQRs].
HbA 1 c (%): hemoglobin A 1 c, a measure of long-term glucose control, UC: usual care group, DE: dietary education group, IQRs: interquartile ranges.

Table 2. Comparison of the effects of the dietary education group and the usual care group

	UC Group		All DE Groups		*P*-value
Body Mass Index (kg/m^2)	24.9	[23.3 - 28.0]	25.7	[22.6 - 29.5]	0.3317
HbA1c (%)	6.8	[6.5 - 7.3]	6.2	[5.8 - 7.0]	0.0007

Mann-Whitney U test were used for comparison analysis. Data are shown as median [IQRs].
HbA 1 c (%): hemoglobin A 1 c, a measure of long-term glucose control, UC: usual care group, DE: dietary education group, IQRs: interquartile ranges.

Effect of HbA 1 c on Seasonal Variation and Dietary Education

Amount of change in HbA 1 c from baseline levels in consecutive of 1 year are shown for the UC group in Figure 1. There were significant differences in HbA 1 c change amount from June to January 2013 : June (−0. 1[−0. 3−0. 1]%, P=0. 0105), July (−0. 1[−0. 4−0. 1]%, P=0. 0021), August (−0. 2[−0. 4−0. 0]%, P<0. 0001), September (−0. 2[−0. 4−0. 0]%, P<0. 0001), October (−0. 2[−0. 4−0. 0]%, P<0. 0001), November (−0. 2[−0. 5−0. 0]%, P<0. 0001), December(−0. 2[−0. 5−0. 0]%, P<0. 0001), and January(−0. 1[−0. 4−0. 1]%, P=0. 0012). However, February(−0. 1[−0. 4−0. 2]%, P=0. 0525), March(0[−0. 4−0. 2]%, P=0. 212), and April (− 0[−0. 3−0. 2]%, P=0. 5922) did not show a significant difference.

To determine any effects on HbA 1 c levels by differences in the timing of the DE intervention, these patients were examined before and following intervention in one of four consecutive calendar quarters, phases 1−4 from April 2013 to March 2014 : phase 1 [April to June, N=10], phase 2 [July to September, N=13]; phase 3 [October to December, N= 7], and phase 4 [January to March, N= 7]. In the phase 1 DE group, June (−0. 45[−0. 8− −0. 1]%, P=0. 0109), July (−0. 75[−1. 2− −0. 3]%, P=0. 0002), August (−0. 85[−1. 3− −0. 4]%, P=0. 0024), September (−0. 75[−1. 20− −0. 2]%, P=0. 0176), November (−0. 5[−1. 4− −0. 3]

%, P=0.0444), February (−0.6[−1.5−0.0]%, P=0.0399), March (−0.7[−1.4−−0.2]%, P=0.0003), and April (−1.0 [−1.4−−0.3] %, P=0.0008) showed significantly decreased HbA1c levels compared with the UC group. Furthermore, HbA1c levels significantly decreased (P<0.05) from June to December and February to April compared with the Phase 1 DE group baseline level (Fig. 1a).

Second, in phase 2 DE group April (−0.3[−0.8−0.1]%, P=0.0483) showed significantly decreased (P<0.05) HbA1c levels compared with the UC group. December HbA1c level significantly decreased compared with the phase 2 DE group baseline (Fig. 2b).

In phase 3 DE group, March (−0.5[−0.7−−0.1]%, P=0.0158) and April (−0.7[−1.3−−0.2]%, P=0.0123) showed significantly decreased HbA1c levels compared with the UC group. Furthermore, the phase 3 DE Group HbA1c levels significantly decreased (P<0.05) in October and March compared with the baseline (Fig. 1c).

HbA1c levels of the phase 4 DE Group were lower than both the baseline level of the phase 4 DE Group (P<0.05) and those of the UC Group (−0.5[−0.7−−0.3]%, P=0.093) in April (Fig. 1d).

Prolonged Effect of the HbA1c Correction by the DE Intervention

This study investigated changes in HbA1c levels an 18-month duration from the start of the DE interventions (Fig. 2). HbA1c levels significantly decreased from the guidance at the start (compared with their baseline) for the first 12 months (P<0.05), but it was not significant thereafter.

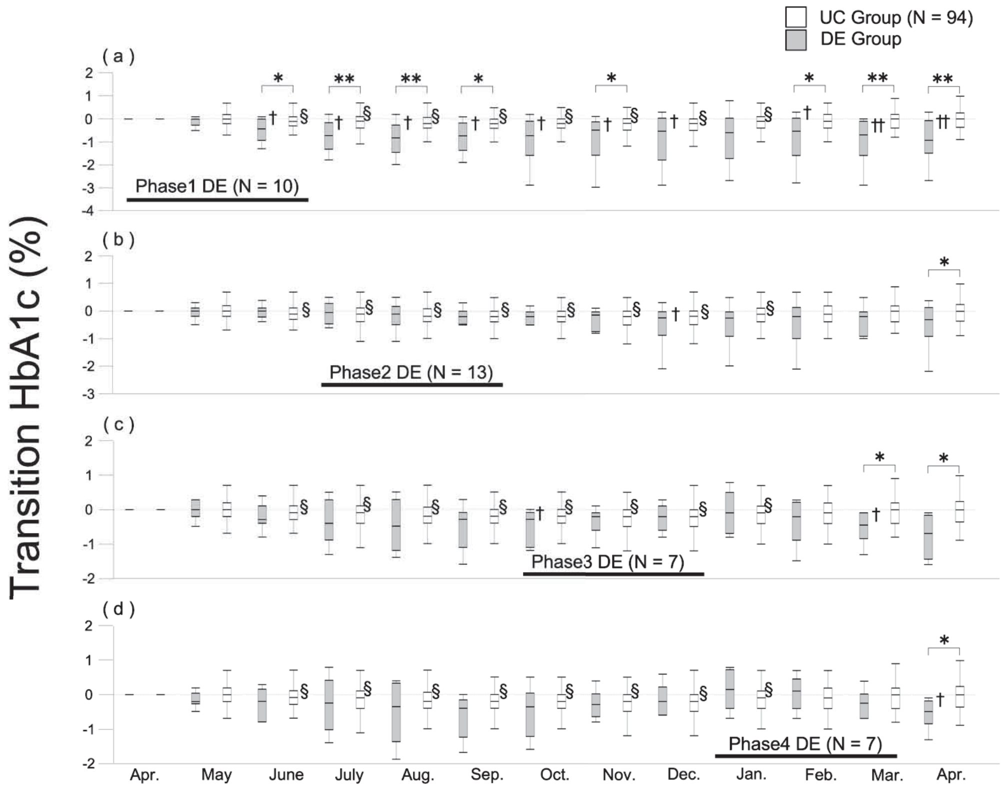

Figure 1 . Change in HbA 1 c from baseline levels by differences in the timing of the DE intervention. The different intervention times (black lines) were (a) phase 1 (April to June), (b) phase 2 (July to September), (c) phase 3 (October to December), and (d) phase 4 (January to March). Data are shown as median, 25th and 75th percentiles. $^{*}P<0.05$, $^{**}P<0.01$ vs. the UC group (Mann-Whitney U test); $^{\dagger}P<0.05$, $^{\dagger\dagger}P<0.01$ vs. the DE group baseline (Wilcoxon signed-rank test); and $^{\S}P<0.05$ vs. the UC group baseline (Wilcoxon signed-rank test).

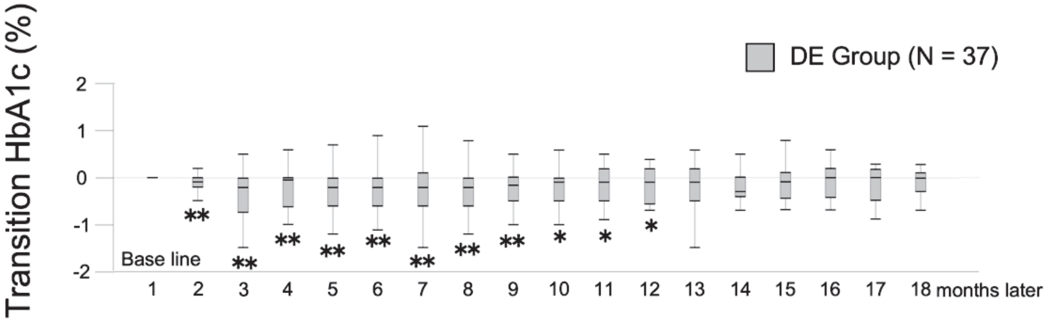

Figure 2 . Prolonged effect of the dietary education. The x-axis was shown the progress of the months. Data are shown as median, 25th and 75th percentiles. $^{*}P<0.05$, $^{**}P<0.01$ vs. baseline (Wilcoxon signed-rank test).

DISCUSSION

At baseline, the patients in the DE group were significantly younger and heavier than those in the UC Group, without a marked difference in HbA 1 c levels (Table 1). The DE corrected their HbA 1 c levels; and BMI was no longer significantly different from the UC Group (Table 2).

Consideration of seasonal variation in HbA 1 c levels in type 2 diabetes mellitus patients demands more effective glycemic control. HbA 1 c levels decrease from summer to autumn, and in winter to spring, they show a tendency to increase. The DE markedly decreased HbA 1 c levels below the respective baseline levels in all four seasons (Fig. 1).

The presence of this seasonal variation in HbA 1 c levels of type 2 diabetes mellitus patients is already known and has been associated with age, sex, region, and insulin administration[5, 6, 18]. In Japanese type 2 diabetes mellitus patients, blood glucose and HbA 1 c levels are low in summer and high in winter and spring. It is believed that the seasonal variation in climate influences appetite; its decline with elevation of the ambient air temperature in summer and its increase with the decrease in the temperature in winter may be the cause of the observed seasonal variation in HbA 1 c levels[6, 19]. The results of this study did not contradict these reports. However, DE intervention corrected HbA 1 c regardless of seasonality.

DE intervention in the phase 1 DE group was able to inhibit baseline increase in HbA 1 c levels (Fig 1 a). Along with the decrease in HbA 1 c in summer, glucose metabolism was effectively improved by providing substantial dietary education. Therefore, an early DE intervention may be important for improving the blood glucose levels of diabetic patients. Patients who gain more knowledge regarding food can better recognize the characteristic appetite-regulating mechanisms of taste, memory, learning, and experience that the effect of DE intervention can contribute to correcting their eating behavior[20, 21]. Although the number of patients in this study was limited, it is suggested that an effect on improving carbohydrate metabolism was obtained by this DE intervention.

Furthermore, a prolonged effect of the DE intervention on glycemic control was obtained for 12 months, but a marked effect was not observed thereafter (Fig. 2). The behavior modification deriving from the DE intervention possibly relapses over time[22]. From this observation, the intervention of periodic education may help the behavior modification persist[23–26]. Our study findings suggest that the abovementioned dietary intervention may be necessary at least once a year. Continuous charting of daily weight and continuous DE may also prove to be important in promoting more effective treatment[14]. These possibilities await further investigation. In addition, it is worth investigating if continuous DE is similarly effective in patients who are treated with insulin and/or oral hypoglycemic medications.

Limitations of this study were the limited number of patients and relatively short period of observation and analysis. These factors must be considered in future studies. In addition, to achieve long-term glycemic control in these patients, annual reinforcement of dietary behavior modification appears to be necessary. In conclusion, the presence of the seasonal variation in HbA 1 c levels was clearly observed in type 2 diabetes mellitus patients. In addition, the DE intervention markedly improved seasonal variation in HbA 1 c and contributed to the carbohydrate metabolism correction of the HbA 1 c levels in the patients.

Acknowledgments

I thank director's INOBE JUN-ICHI of the Inobe Hospital, who supported this study.

Conflicts of interest

I have no disclosure and financial support.

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【要旨】

日本の糖尿病患者の糖代謝には季節変動が存在する。本研究は、栄養食事指導の介入による２型糖尿病患者の HbA１c の季節変動の有無を検討した。HbA１c の季節変動は、２型糖尿病患者において存在し、その推移は夏と秋の間に減少、冬と春に増加を示した。栄養食事指導は、介入する季節性に関係なく、HbA１c を低下させ、より効果的に糖代謝を是正した。