A Prospective Study of Glycemic Control During Holiday Time in Type 2 Diabetic Patients

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OBJECTIVE — In the U.K. Prospective Diabetes Study, A1C increased from 1.2 to 1.7% and fasting plasma glucose from 1.0 to 2.8 mmol/l over 10 years in type 2 diabetic patients. It is not known whether the blood glucose increase observed in long-term studies of type 2 diabetes results from small, steady increases throughout the year or from increases during discrete periods.

RESEARCH DESIGN AND METHODS — To estimate the variation of actual glycemic control and its relation to holiday times, we measured A1C and fructosamine in 110 patients with type 2 diabetes. These measurements were performed four times at intervals of 4–6 weeks; therefore, glycemic change was determined for three periods: preholiday period (from between November 13 and December 20 to between December 20 and January 20), holiday period (from between December 20 and January 20 to between January 28 and February 28), and postholiday period (from between January 28 and February 28 to between March 1 and April 10). A final measurement of A1C was obtained from 90 subjects in the following December or January.

RESULTS — The mean A1C increased, but not significantly, during the preholiday (increase 0.135 ± 0.723%, $P = 0.055$) and holiday (increase 0.094 ± 0.828%, $P = 0.239$) periods. The mean A1C decreased, but not significantly, during the postholiday period (decrease 0.022 ± 0.588%, $P = 0.695$). Altogether, the A1C change during these three periods increased significantly (increase 0.207 ± 0.943%, $P = 0.024$). The mean fructosamine increased significantly during the preholiday period (increase 0.151 ± 0.460 mmol/l, $P = 0.001$), but there was no significant change during the holiday period (increase 0.057 ± 0.593 mmol/l, $P = 0.321$). However, fructosamine decreased significantly during the postholiday period (decrease 0.178 ± 0.448 mmol/l, $P < 0.001$). Altogether, the fructosamine changes during the study periods showed no significant difference (increase 0.030 ± 0.566 mmol/l, $P = 0.579$). Between March or early April and the following December or January, there was no additional change in A1C (decrease 0.009 ± 1.039%, $P = 0.935$) for the 90 participants who returned for follow-up treatment.

CONCLUSIONS — The present study demonstrates an influence of winter holidays on the glycemic control of patients who have type 2 diabetes, and this poor glycemic control might not be reversed during the summer and autumn months. Therefore, the cumulative effects of the yearly A1C gain during the winter holidays are likely to contribute to the substantial increase in A1C that occurs every year among type 2 diabetic individuals.

Diabetes Care 27:326–330, 2004

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Received for publication 17 June 2003 and accepted in revised form 23 October 2003.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Poor glycemic control in type 2 diabetes has serious consequences for health and is a major risk factor for the development of diabetes complications. Good control of blood glucose concentration leads to fewer complications (1). From the U.K. Prospective Diabetes Study data, A1C increased from 1.2 to 1.7% and fasting plasma glucose from 1.0 to 2.8 mmol/l over 10 years in type 2 diabetic subjects (1). It is not known whether the blood glucose increase observed in long-term studies of type 2 diabetes results from small, steady increases throughout the years or from increases during discrete periods of increased energy intake, decreased energy expenditure, or both, such as during holiday periods or particular seasons.

The balance between dietary intake and energy consumption through daily physical activities is the most influential factor in the glycemic control of type 2 diabetic patients (2). The nutritional prescription made for a diabetic individual is usually determined by taking into consideration expected physical activity, diabetes complications, and age (2). Seasonal variation of glycemic control in diabetes has been reported in some previous studies (3–7), but no Chinese data are available. This study seeks to investigate some effects of cultural variation on glycemic control, using the case of Chinese holidays. For the Chinese, the winter holiday season is generally considered to begin with the winter solstice (December 23) and end after the Lantern Festival (in February). During the winter holidays, people are customarily physically inactive and they enjoy salty meals and alcoholic beverages. This often leads to weight gain and may be a factor in the increased levels of A1C found every year among type 2 diabetic subjects.

To determine the effect of both the season and the holiday period on changes of glycemic control in Chinese type 2 diabetic subjects, we measured and calculated the individual changes of the following factors before, during, and after the winter holiday season from November

Table 1—*Selected variables at every visit*

	Visit 1: between November 13 and December 20	Visit 2: between December 20 and January 20	Visit 3: between January 28 and February 28	Visit 4: between March 1st and April 10	*P**
n (M/F)	110 (83/27)	109 (83/26)	109 (83/26)	108 (82/26)	
Body weight (kg)	67.67 ± 9.40	67.71 ± 9.49	67.69 ± 9.47	67.71 ± 9.50	NS
Systolic blood pressure (mmHg)	139.0 ± 17.7	141.5 ± 17.0	145.9 ± 19.3	144.2 ± 17.6	*, †, ‡
Diastolic blood pressure (mmHg)	75.2 ± 11.8	76.6 ± 11.9	79.1 ± 11.4	78.8 ± 11.3	*, †, ‡, §
Pulse rate (bpm)	79.8 ± 12.0	81.5 ± 12.0	81.3 ± 11.6	80.9 ± 12.2	NS
Fasting plasma glucose (mg/dl)	160.5 ± 35.9	163.0 ± 33.0	166.1 ± 37.4	170.1 ± 56.2	NS
A1C (%)	7.308 ± 1.294	7.444 ± 1.277	7.538 ± 1.352	7.516 ± 1.372	*, †
Fructosamine (mmol/l)	2.968 ± 0.556	3.119 ± 0.575	3.176 ± 0.518	2.998 ± 0.482	*, †, ‖, ¶

Data are means ± SD. *$P < 0.05$, visit 1 vs. 3; †$P < 0.05$, visit 1 vs. 4; ‡$P < 0.05$, visit 2 vs. 3; §$P < 0.05$, visit 2 vs. 4; ‖$P < 0.05$, visit 1 vs. 2; ¶$P < 0.05$, visit 3 vs. 4, NS, not significant.

to March: plasma glucose, A1C, and fructosamine.

RESEARCH DESIGN AND METHODS

— A total of 110 subjects with type 2 diabetes were recruited for the study after informed consent was obtained. The study was conducted from October 2000 to April 2001 in Taipei Veterans General Hospital. Eligible participants were aged 30–80 years, had type 2 diabetes, and were treated with oral antidiabetic drugs. Their progress was followed-up in our hospital for at least 6 months and for as long as subjects were willing to attend all study visits. Subjects were excluded if they had late complications of diabetes, were taking insulin for glycemic control, or were pregnant.

In this study, the Chinese New Year's holiday was from January 20 to 28 in 2001 for 9 days. During this time, most people do not have to work. Blood samples were taken from subjects on four occasions at intervals of 4–6 weeks. Visit 1 was between November 13 and December 20, visit 2 between December 20 and January 20 (before Chinese New Year's Day [23 January 2001]), visit 3 between January 28 and February 28, and visit 4 between March 1 and April 10. The preholiday period was defined as from visit 1 to 2, the holiday period as visit 2 to 3, and the postholiday period as visit 3 to 4. Therefore, glycemic change was determined for three periods: preholiday period (from between November 13 and December 20 to between December 20 and January 20), holiday period (from between December 20 and January 20 to between January 28 and February 28), and postholiday period (from between January 28 and February 28 to between March 1 and April 10). At every clinic visit, fasting whole blood was taken for plasma glucose (NaF), fructosamine (EDTA), and A1C (EDTA) assays. We also measured the subjects' body weight, blood pressure, and pulse rate at every visit and their body height at the first visit. Plasma glucose was measured using the glucose oxidase method with a glucose analyzer (Model 2300; YSI, Yellow Spring, OH). A1C was measured using high-performance liquid chromatography instruments (HLC-723 GHB IIIs; Tosoh, Tokyo, Japan), with a reference range of 4.2–5.8%. The interassay with between-batch coefficient of variance (CV) was <2.0% at mean A1C levels between 4.4 and 8.2%. Fructosamine was measured using the Glyco-probe (Drawer 4350; Isolab, Akron, OH), with a reference range of 1.6–2.4 mmol/l. The interassay CV was 4.2% at 1.4 mmol/l and 5.6% at 3.1 mmol/l ($n = 50$). The subjects were weighed wearing clothes without shoes in the morning after breakfast to the nearest 0.01 kg with an electronic scale. Blood pressure and pulse rate were taken by an electronic sphygmomanometer in the sitting position after 10 min of rest. Height was measured to the nearest 1 cm with a stadiometer.

The subjects were subsequently invited to return in December 2001 or January 2002 before the next Chinese New Year's Day. They were observed for glycemic control over a 1-year period.

Statistical analysis

SPSS for Windows, version 10.0, was used for data analysis. Glycemic control data from the four measurements were used to compute A1C and fructosamine change for the three periods: preholiday, holiday, and postholiday. Paired *t* tests were used to determine the differences in glycemic control among the three periods, and blood pressure, pulse rate, and body weight were used to determine differences between the baseline and postholiday periods. Data are presented as means ± SD unless otherwise stated, and a *P* value <0.05 was taken to indicate a significant difference.

RESULTS

— A total of 110 subjects with type 2 diabetes were recruited for the study, and complete data from the four visits were available for 108 patients (98.2%). Their mean age was 67.4 ± 9.4 years (95% CI 65.7–69.2) and mean diabetes duration 7.7 ± 5.8 years (95% CI 6.6–8.8). Seventy-five percent of subjects were men. Some demographic data on the 110 recruited subjects are presented in Table 1. The glycemic control between measurements was also calculated using two models: model 1 ($n = 106$) eliminated 2 subjects who were admitted to hospital for surgery or fracture, and model 2 ($n = 96$) further eliminated 10 subjects whose oral antidiabetic drug dosage was changed during these periods. Although the results were unchanged when the two methods of analysis were used, the adjusted analysis is still currently presented.

The absolute values of A1C and fructosamine at each visit are shown in Table 1. Figure 1 reveals the A1C change during the study period. The mean A1C increased, but not significantly, during the preholiday (change 0.135 ± 0.723% [95% CI −0.027 to 0.273] [negative

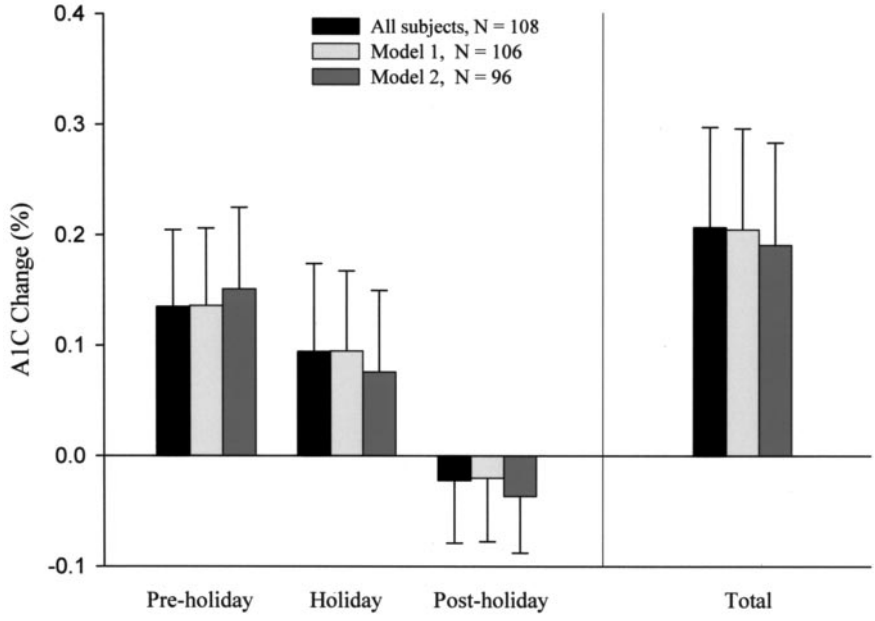

Figure 1—*A1C change during the study period.*

numbers indicate decrease], $P = 0.055$) and holiday (change 0.094 ± 0.828% [95% CI −0.063 to 0.252], $P = 0.239$) periods. The mean A1C decreased, but not significantly, during the postholiday period (change −0.022 ± 0.588% [95% CI −0.134 to 0.090], $P = 0.695$). The sum of the A1C change during these three periods increased significantly (change 0.207 ± 0.943% [95% CI 0.028–0.387], $P = 0.024$). The A1C change in both model 1 and 2 subjects revealed similar results to those in all subjects.

Figure 2 shows the fructosamine change during the study period. The mean fructosamine increased significantly during the preholiday period (change 0.151 ± 0.460 mmol/l [95% CI 0.063–0.239], $P = 0.001$) and increased, but not significantly, during the holiday period (change 0.057 ± 0.592 mmol/l [95% CI −0.056 to 0.170], $P = 0.321$). However, fructosamine decreased significantly during the postholiday period (change −0.178 ± 0.448 mmol/l [95% CI −0.263 to −0.092], $P < 0.001$). The total fructosamine change during the study periods showed no significant difference (change 0.030 ± 0.566 mmol/l [95% CI −0.078 to 0.092], $P = 0.579$). The fructosamine change during the study period among both model 1 and 2 subjects revealed the same results as those in all subjects.

Some selected variables that were measured during the study period are shown in Table 1. Body weight, pulse rate, and fasting plasma glucose did not reveal significant differences between the two visits. Both the systolic and diastolic blood pressures increased significantly from visit 1 to 3, visit 2 to 3, and visit 1 to 4. Diastolic blood pressures also increased from visit 2 to 4. Table 2 reveals subjects' characteristics between patients with poor and good glycemic control. Of our measurements, only diabetes duration shows significant difference between the highest and lowest quartile.

A subgroup of 90 subjects (81.8%) agreed to return for an additional visit between the following December and January. Their average holiday A1C changes were 0.198 ± 1.056% (95% CI 0.026–0.421, $P = 0.028$). These were not significantly different from those who did not choose to return. Between March or early April and the following December or January, their net change in A1C was a loss of 0.009 ± 1.039% (95% CI −0.211 to 0.229, $P = 0.935$), leading to a net A1C gain of 0.189 ± 0.807% (95% CI 0.018–0.036, $P = 0.045$) during the 1-year observation period.

CONCLUSIONS — The data from our study indicate an influence of the winter holiday on the glycemic control of type 2 diabetic subjects. These results also demonstrate that this poor glycemic control might not be reversed during the summer and autumn months. Therefore, the cumulative effects of the yearly A1C gain during the winter holidays are likely to contribute to the substantial increase in A1C that frequently occurs among type 2 diabetic subjects. These may be caused by a seasonal change of glycemic control and could result in a markedly increased blood glucose levels in a few years. Interestingly, these subjects can notice their poor glycemic control in the preholiday

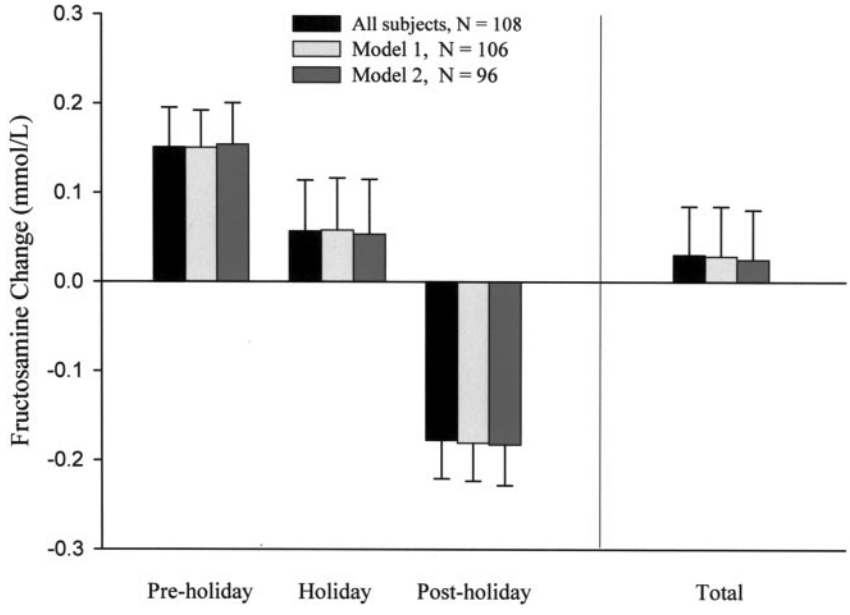

Figure 2—*Fructosamine change during the study period.*

Table 2—*Initial characteristics of different glycemic control according to A1C change during the holiday period*

	Highest quartile of glycemic control	Lowest quartile of glycemic control	*P*
n	28	27	
Sex (M/F)	17/11	20/7	0.061
Age (years)	67.1 ± 7.8	69.5 ± 7.9	0.273
Diabetes duration (years)	6.1 ± 4.1	11.4 ± 7.6	0.004
Developing age (years)	61.0 ± 9.2	58.4 ± 9.8	0.318
Body height (cm)	162.4 ± 8.0	165.5 ± 8.9	0.217
Body weight (kg)	66.15 ± 9.55	68.62 ± 8.92	0.326
BMI (kg/m^2)	25.41 ± 3.85	24.76 ± 2.83	0.555
Systolic blood pressure (mmHg)	138.2 ± 16.8	142.6 ± 17.5	0.351
Diastolic blood pressure (mmHg)	73.3 ± 12.8	75.1 ± 12.8	0.614
Pulse rate (bpm)	80.7 ± 12.9	76.5 ± 11.3	0.208
Fasting plasma glucose (mg/dl)	170.4 ± 39.8	158.7 ± 41.4	0.252
A1C (%)	7.39 ± 1.35	7.21 ± 1.41	0.461
Fructosamine (mmol/l)	3.023 ± 0.548	3.029 ± 0.603	0.970
A1C change (%)	−0.843 ± 0.501	+1.248 ± 0.441	<0.001
Fructosamine change (mmol/l)	−0.107 ± 0.502	+0.034 ± 0.689	0.394

Data are means ± SD. −, decrease; +, increase.

and holiday periods and attempt to improve their glycemic control in the postholiday period. Unfortunately, however, the accumulated high blood glucose concentrations reflected from the A1C levels cannot be recovered in the postholiday period. Our results also suggest that the winter holiday season may present special risk for those who had longstanding diabetes, indicating that such patients may benefit from seasonal efforts to prevent poor glycemic control.

A1C measurements in our study subjects increased slightly during the Chinese New Year's holiday, which is likely due to the common perception that there is relatively poor glycemic control during the winter holiday season (3–7). We found that the 0.135% average A1C gain during the preholiday period and the 0.094% increase during the holiday period were largely maintained during the postholiday winter period from February to March, resulting in a net average A1C gain of 0.207%. In subjects who completed 1 year of observation, the A1C increased by an average of 0.198% during the holiday period and decreased 0.009% over the entire year, suggesting that the period contributing most to the yearly A1C change is this holiday period. Unlike the A1C change, measurements of fructosamine in these subjects changed more variably during the winter holiday period. We found that there was a 0.151-mmol/l average fructosamine increase during the preholiday period and a 0.057-mmol/l gain during the holiday period; however, there was a decrease of 0.178 mmol/l during the postholiday period. This results in a net average fructosamine gain that is not significant (0.030 ± 0.566 mmol/l, $P = 0.579$). For diabetic subjects, a serum fructosamine assay can better reflect the average blood glucose concentration over the previous 3–6 weeks and A1C can better reflect the previous 8–10 weeks (8). These results clearly reflect relatively poor glycemic control in the preholiday and holiday periods and good glycemic control in the postholiday period. However, poor glycemic control, based on measurement of A1C, does not return to preholiday levels during the postholiday periods despite relatively good glycemic control in this period.

Few prior studies have evaluated the variation in glycemic control during holiday periods or particular seasons in diabetic subjects (3–7). Some previous studies revealed seasonal variations in glycemic control in diabetic subjects, and they generally came to similar broad conclusions. Asplund (3) studied 800 diabetic subjects in Sweden and found a peak A1C level between January and April and a nadir between June and August. Ishii et al. (6) examined a small number of Japanese subjects with type 2 diabetes ($n = 39$), and found that their mean A1C level was elevated by ~0.5% in winter compared with the period between spring and autumn. Similarly, Maguire and Edward (7) studied 1,295 British diabetic subjects at ~3-month intervals over a 2-year period. Their study showed a seasonal variation in glycemic control, with a maximum in the spring (March, April, and May) and a nadir in the autumn (September, October, and November). However, unlike our present study, their study subjects were not investigated during the same period, they had no regular follow-up intervals, and they used heterogeneous subjects. We investigated homogenous subjects (type 2 diabetes without insulin therapy); they were observed in the same period and were followed-up regularly at the same intervals. The present study not only confirms the overall existence of a significant difference in the seasonal pattern of glycemic control, but it also shows a cumulative effect of blood glucose level during the winter holidays.

Although blood pressure was not our primary outcome, our data revealed the significance of systolic and diastolic blood pressure change during some time points (Table 1). The blood pressure change could also be explained by the fact that people are customarily physically inactive and they enjoy salty meals and alcoholic beverages during the winter holidays. This often leads to increased blood pressure and blood glucose level.

Poor glycemic control in type 2 diabetic patients has serious consequences for health and is a major risk factor for the development of diabetes complications. The 0.207% A1C gain of the subjects in this study between November and March or early April might not appear to be clinically important and could easily go unnoticed by both subjects and physicians. Since this gain might not be reversed during the summer and autumn months, the net 0.207% A1C increase in the holiday period probably contributes to the increased A1C level of up to 2% over 10 years. Notwithstanding the reasons, the observed holiday change in diabetes control has important implications for the interpretation of A1C results and, consequently, in the management of diabetic patients.

Acknowledgment— This study was supported by a grant for Medical Research (VGH-89057 and VGH-90047) from the Taipei Veterans General Hospital, Taiwan.

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