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ORIGINAL ARTICLE

Randomized controlled trial for an effect of green tea-extract powder supplementation on glucose abnormalities

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Objective: We examined whether green tea-extract powder supplementation improves glucose abnormality.
Methods: The study was conducted for volunteers who resided in eastern communities of Shizuoka Prefecture and who had fasting blood glucose levels of $\geqslant$6.1 mmol/l or nonfasting blood glucose levels of $\geqslant$7.8 mmol/l in a recent health check-up. Sixty subjects aged 32–73 years (49 males and 11 females) participated in the trial. The Early intervention group consumed a packet of green tea-extract powder containing 544 mg polyphenols (456 mg catechins) daily for the first 2 months and then entered the 2-month nonintervention period. The Later intervention group was observed for the first 2 months and then consumed green tea-extract powder as described above for the subsequent 2 months. Using the two-period crossover design, we analyzed the changes in fasting hemoglobin A1c level and other biomarkers in blood samples collected at baseline, 2 months and 4 months.
Results: A significant reduction in hemoglobin A1c level and a borderline significant reduction in diastolic blood pressure were associated with the intervention. The intervention caused no significant changes in weight, body mass index, body fat, systolic blood pressure, fasting serum glucose level, homeostasis model assessment index, serum lipid level or hypersensitive C-reactive protein.
Conclusion: Daily supplementary intake of green tea-extract powder lowered the hemoglobin A1c level in individuals with borderline diabetes.
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Keywords: green tea consumption; polyphenol; nutrition; hemoglobin A1c; diabetes; randomized-controlled trial

Introduction

Green tea polyphenols have physiologic activities such as anticancer effects (Hara *et al*., 1989; Isemura *et al*., 1993; Muramatsu, 1994; Ito and Sasaki, 1995; Suganuma and Okabe, 1996; Dreosti *et al*., 1997; Imai *et al*., 1997), antioxidative activity (Kawase *et al*., 2000; Yokozawa *et al*., 2000), antibacterial effects (Sakanaka *et al*., 1989; Mabe *et al*., 1999; Amarowicz *et al*., 2000), antioxidative activity against low-density lipoprotein cholesterol (Rice-Evans *et al*., 1996; Miura *et al*., 2000), and reduction of blood cholesterol level (Muramatsu *et al*., 1986; Imai and Nakachi, 1995), body weight, body fat (Hase *et al*., 2001; Nagao *et al*., 2001; Tsuchida *et al*., 2002; Kajimoto *et al*., 2005), blood glucose level (Hara and Honda, 1990; Honda and Hara, 1993; Matsumoto *et al*., 1993) and suppression of postprandial triglyceride elevation (Unno *et al*., 2005). Therefore, it is expected that green tea polyphenols have preventive effects against lifestyle-related diseases. However, there have been few nutritional epidemiological studies on the influence of green tea consumption on human health (Fukino *et al*., 1999), and the beneficial effects of green tea ingredients in preventing and controlling diabetes and cardiovascular disease have not been well elucidated.

Studies on the effect of lifestyle changes such as body weight loss, an increase in physical activity and improvement of diet demonstrated that they led to reduced incidence of type II diabetes (Tuomilehto *et al*., 2001; Diabetes Prevention Program Research Group, 2002). In

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Japan, the proportions of individuals with diabetes or borderline diabetes have increased (Ohmura *et al*., 1993; Ministry of Health, Labour and Welfare, Japan, 2004), indicating the need for further research on prevention and control of diabetes.

Our aims were to investigate the influence of consumption of a supplement of green tea-extract powder on polyphenol intake and biomarkers of glucose metabolism and to clarify whether consumption of the supplement improves glucose abnormalities in a randomized-controlled crossover trial. We reported a preliminary result for the first half part of our crossover trial: subjects in the first group took the supplement of green tea-extract powder containing polyphenol 544 mg (total catechin 456 mg) daily for 2 months, while they in the second group were simply observed (Fukino *et al*., 2005). In this paper, we report the final results of the 4-month crossover trial.

Methods

Subjects and crossover randomized trial design

The subjects were volunteers who were residents of eastern communities of Shizuoka Prefecture, Japan, who had a fasting blood glucose level of >6.1 mmol/l or a nonfasting blood glucose level of >7.8 mmol/l in a recent health check-up. We asked individuals to participate in this study, and obtained informed consent from 56 males and 14 females aged 32–73 years. After excluding 10 subjects who quit study participation ($n=9$) or who had eaten breakfast at the baseline data sampling ($n=1$), the final number of subjects was 49 for males and 11 for females (Figure 1). Seven subjects in the Early intervention group and nine subjects in the Later intervention group were on medication for diabetes mellitus at the baseline survey. No subjects took dietary supplement in either intervention group. The design of present study was a crossover randomized control trial without blinding or washout period. This study was approved by the Research Ethics Committee of Shizuoka Prefecture University.

The first venous blood sample was obtained at baseline between late February and early March 2003, and two additional venous blood samples were obtained at 2 and 4 months. The subjects were randomly divided into the Early intervention group or Later intervention group. The subjects in the Early intervention group were asked to take one packet of the supplement daily during the first 2 months of the study, while the subjects in the Later intervention group were asked to take one packet of the supplement daily during the third and fourth months of the study. The supplement was composed of a mixture of green tea-extract and green tea powder at a ratio of 9:1. One packet of the supplement contained a total of 544 mg polyphenols (456 mg catechins) and 102 mg caffeine, and can be consumed daily without difficulty. The subject was asked to drink 1/3 to 1/4 of the content of a packet dissolved in hot water at the end of every meal or snack (one packet per day). The subjects had kept a record on the intake of green tea-extract powder supplement during the intervention period. In both groups, data were collected at baseline, 2 and 4 months, and changes in biomarkers were analyzed.

A unique feature of this study was that we studied the amount and concentration of green tea that each subject usually consumes, and calculated the amount of polyphenol intake. In addition, we examined whether the supplement of green tea-extract powder has beneficial effects on physical measurements and blood chemistry parameters.

Measurement of biochemical markers

We measured blood pressure, height, body weight, biochemical data on fasting blood glucose, insulin and hemoglobin A1c at baseline, 2 and 4 months, and conducted an oral

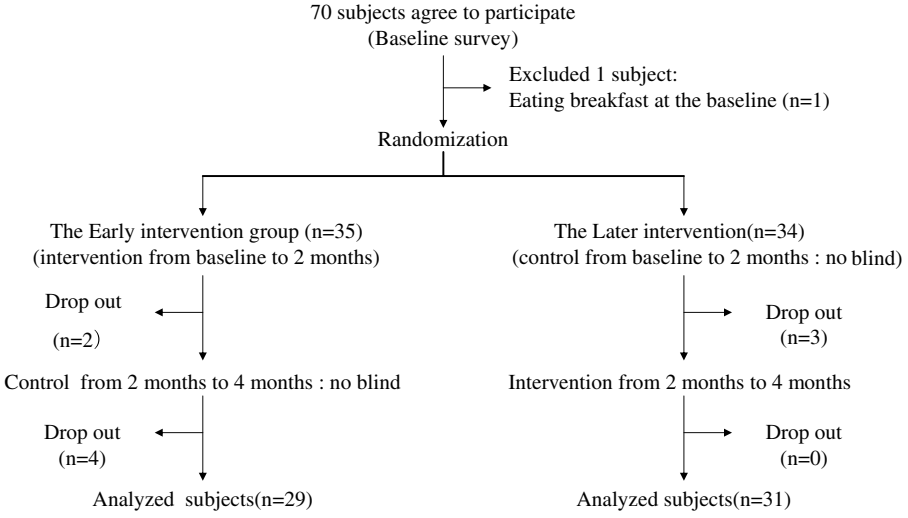

Figure 1 Sampling scheme for the study.

questionnaires survey on health, lifestyle and nutrition, as well as concentration of green tea and frequency of green tea consumption.

For measurement of the serum lipid and glucose levels, venous blood was drawn from the seated participant into a plain, siliconized glass tube, and the serum was separated within 30 min. The serum sample was transported on dry ice to the Osaka Medical Central for Health Science and Promotion, an international member of the US National Cholesterol Reference Method Laboratory Network, and stored at −70°C until measurement. The serum triglyceride level was also measured by an enzymatic method, and the serum total cholesterol and high-density lipoprotein cholesterol levels were measured using enzymatic methods by an automatic analyzer (Hitachi 7250; Hitachi Medical Corp., Hitachi, Japan). The serum glucose level was measured by the hexokinase method using the same instrument. The hemoglobin A1c level was measured by a latex agglutination immunoassay using the Determiner HbA1c kit (Kyowa Medex Co., Ltd, Tokyo, Japan) and an automatic analyzer (Chemistry Analyzer AU2700; Olympus Medical Engineering Company, Tokyo, Japan). Serum high-sensitive C-reactive protein levels were measured by latex particle-enhanced immunonepherometric assay (BN Pro Spec; Dade Behring Inc., IL, USA).

Body mass index (BMI) was calculated as body weight (kg) divided by the square of the height of the individual ($(m)^2$). The homeostasis model assessment (HOMA) index was calculated as fasting blood glucose level (mg/dl) multiplied by fasting insulin level (μU/ml)/405.

Measurement of green tea polyphenol content and calculation of polyphenol intake

The polyphenol content in green tea-extract powder was measured by colorimetry with a ferric tartrate reagent (Iwase *et al*., 1970). The sample (30 mg) was suspended in 50–60 ml of deionized water in a 100 ml measuring flask, which was placed in a hot water bath of a temperature of above 80°C. After the powder was completely dissolved, the solution was cooled and the volume was adjusted to 100 ml. The solution was filtrated. Five milliliters of the sample solution and 5 ml of ferric tartrate reagent were combined and the volume was adjusted to exactly 25 ml by adding phosphate buffer. This was mixed well for preparation sample of coloration. After mixture, absorbance was measured using colorimetry at 540 nm wavelength, and a calibration curve was obtained using water as the control. Ethyl gallate was used as the standard sample and a calibration curve was plotted. The concentration (C) of ethyl gallate and the total content of polyphenols in the sample were determined by the following equation: total polyphenol content (%) $= (C/W) \times 1.5 \times 100$, where W is the weight of the sample (mg) and C is the concentration of ethyl gallate in the sample solution as determined by the calibration curve (mg/100 ml).

The amount of daily intake of polyphenols from green tea was estimated from the daily intake of green tea multiplied by the concentration of green tea that the subject usually drinks, and during the intervention the amount of polyphenols from the supplement was added. The concentration of green tea that the subject usually drinks was judged by administering a taste test of 3 concentrations of green tea, that is, 1, 2 and 3%, that had been prepared by extracting a given amount of tea in hot water at 85°C for 1 min. We aimed to obtain the better estimate for the intake of green tea polyphenols, using the chemical data on the amount of polyphenols per 100 ml of green tea (for example, 40 mg polyphenols per 100 ml 1% green tea) and supplemental green tea powder (544 mg polyphenols per packet) as well as the interview survey data on the concentration and frequency of green tea intake.

The formula for polyphenols intake (mg per day) is (the frequency of green tea (cups per day)) × (the amount of green tea polyphenols per 100 ml of green tea) + (the amount of polyphenols from the supplement).

Measurement of other nutrient intake

Nutrition surveys were carried out by 24-h dietary recall (Kojima and Takakuwa, 1987) at baseline, 2 and 4 months. The subjects were interviewed on what they had eaten during the 24-h period before the interview. Four registered nutritionists (YF *et al*.) carried out the interviews based on the dietary recall manual of our department.

During the interviews, actual-sized food models, pictures of food materials and dishes and/or real foods and dishes were shown so that the subjects could easily recall what they had eaten. The same basic food models and interview forms were used throughout the surveys. As for rice and miso soup, we asked the subject to put the amount of rice and miso soup that he or she usually eats into a bowl and then measured the quantity. We also investigated the frequency of consumption of 18 major foods and food groups per week to confirm that the foods in the 24-h dietary recall did not significantly differ from the foods that the subject usually eats.

The dietary recall interview took approximately 30 min. Intake of nutrients was estimated based on the Standard Tables of Food Composition in Japan (fifth revised edition) (Science and Technology Agency, 2000).

Statistical analysis

Analysis of variance for a crossover design was performed for each variable of interest including polyphenol intake, intake of other nutrients, BMI and biochemical markers with a general linear model. The subject effect, carryover effect (a term for intervention received in the previous intervention period), intervention effect (supplement vs no supplement) and period effect were tested in a one-sided test at 5% level of significance, because we had *a priori* hypothesis that biomarkers for glucose metabolism would be changed by

the green tea-extract supplementation. All statistical analyses were performed with SAS software (version 8.2; SAS Institute Inc., Cary, NC, USA).

Results

Table 1 shows the baseline characteristics of the Early intervention and Later intervention groups. The proportion of men was approximately 85% in both groups. The age and other baseline characteristics did not significantly differ between the two groups.

Table 2 shows the intakes of polyphenol and other nutrients in the Early and Later intervention groups at baseline, 2 and 4 months. There was a substantial increase in polyphenol intake from the supplementation of green tea-extract powder. The mean daily polyphenol intake at baseline, 2 and 4 months in the Early intervention group was 441, 693 and 381 mg, respectively, and that in the Later intervention group was 292, 466 and 700 mg, respectively (Figure 2). The intakes of energy, protein, fat, carbohydrates and other nutrients except for sodium chloride were comparable at each time point between the two groups. Sodium chloride intake significantly increased during the intervention.

Table 3 shows the main outcome measures for the glucose metabolism, physical and other biochemical measures of the Early and Later intervention groups at baseline, 2 and 4 months. There was a significant reduction in the hemoglobin A1c level associated with the intervention. The mean HbA1c level at baseline, 2 and 4 months was 6.2, 5.9 and 5.8%, respectively in the Early intervention group, and 6.1, 6.1 and 5.9%, respectively in the Later intervention group (Figure 3). The reduction in diastolic blood pressure associated with the intervention was of borderline statistical significance. There were no significant changes in weight, BMI, body fat, systolic blood pressure, fasting serum glucose

Table 1 Baseline characteristics of Early and Later intervention groups

Baseline variable	*Early intervention (n = 29)*	*Later intervention (n = 31)*
Age (years)	53.9±8.6	53.4±7.7
Men (%)	86.2	83.9
Weight (kg)	68.3±14.6	70.2±12.2
Body mass index (kg/m^2)	25.4±5.0	26.0±4.1
Systolic blood pressure (mm Hg)	137.9±14.8	137.6±17.5
Diastolic blood pressure (mm Hg)	91.7±10.5	87.0±11.0
Fasting serum glucose (mmol/l)	7.6±3.5	7.7±2.5
Hemoglobin A_{1c} (%)	6.2±2.0	6.1±1.3
Fasting serum insulin (μU/ml)	8.8±7.3	10.3±10.1
HOMA	3.0±2.9	3.7±4.4
C-reactive protein (μg/dl)	110±109	123±163
Polyphenol intake (mg/day)	441±267	292±179
Ethanol intake (g/day)	17.8±28.1	20.5±18.0

Abbreviation: HOMA, homeostasis model assessment.
Values are expressed as mean±s.d. or percentage.

Table 2 Changes in polyphenol and nutrient intake between the Early and Later intervention groups

	Baseline	*After 2 months*	*After 4 months*	P
Polyphenol intake (mg/day)				
Early intervention	441±267	693±216	381±212	<0.001
Later intervention	292±179	466±344	700±295	—
Nutrient intake				
Total energy (kcal/day)				
Early intervention	2036±663	1925±589	1875±410	0.38
Later intervention	2038±554	2085±548	2093±556	—
Total protein (g/day)				
Early intervention	80.4±22.4	78.0±22.9	69.6±16.9	0.27
Later intervention	83.1±22.5	80.0±21.4	78.2±26.6	—
Total fat (g/day)				
Early intervention	53.1±29.2	53.8±21.8	50.7±18.5	0.32
Later intervention	65.0±28.7	60.8±21.1	58.7±25.6	—
Carbohydrate (g/day)				
Early intervention	288.7±116.6	250.2±89.0	262.8±67.8	0.10
Later intervention	240.8±72.7	257.2±88.2	275.4±67.5	—
Insoluble dietary fiber (g/day)				
Early intervention	11.9±4.1	9.7±4.6	9.1±3.8	0.20
Later intervention	12.0±4.6	8.6±3.5	8.3±2.4	—
Total dietary fiber (g/day)				
Early intervention	16.8±5.8	13.7±6.7	13.5±5.3	0.14
Later intervention	17.5±6.5	12.1±4.9	12.7±4.9	—
Sodium chloride (g/day)				
Early intervention	10.5±3.9	11.3±4.2	8.9±3.3	0.01
Later intervention	12.3±3.8	11.1±3.5	12.0±3.6	—
Potassium (mg/day)				
Early intervention	3098±1037	2768±1002	2727±732	0.36
Later intervention	3235±964	2812±860	2804±695	—
Calcium (mg/day)				
Early intervention	596±257	515±314	459±240	0.29
Later intervention	621±261	524±240	559±288	—
Magnesium (mg/day)				
Early intervention	344±96	308±112	298±86	0.41
Later intervention	364±96	317±102	312±75	—
Iron (mg/day)				
Early intervention	11.6±3.8	10.0±3.8	10.1±4.3	0.46
Later intervention	12.2±4.0	10.1±3.1	9.7±2.9	—
Zinc (mg/day)				
Early intervention	8.8±3.0	8.7±3.4	7.8±2.7	0.14
Later intervention	10.4±4.8	8.7±3.1	8.4±2.3	—
Copper (mg/day)				
Early intervention	1.4±0.5	1.4±0.8	1.3±0.4	0.26
Later intervention	1.5±0.4	1.3±0.5	1.3±0.3	—
Carotin (μg/day)				
Early intervention	4752±4115	3620±3088	2414±2035	0.10
Later intervention	4509±3256	2227±1726	2153±1890	—
Vitamin E (mg/day)				
Early intervention	8.6±3.7	8.4±3.4	7.7±3.4	0.13
Later intervention	11.3±4.9	8.9±3.8	7.9±3.2	—
Vitamin K (μg/day)				
Early intervention	401±312	308±241	242±189	0.13
Later intervention	444±285	241±170	206±146	—
Vitamin C (mg/day)				
Early intervention	180±118	125±64	119±62	0.29
Later intervention	161±78	138±53	132±87	—

Values are expressed as mean±s.d.

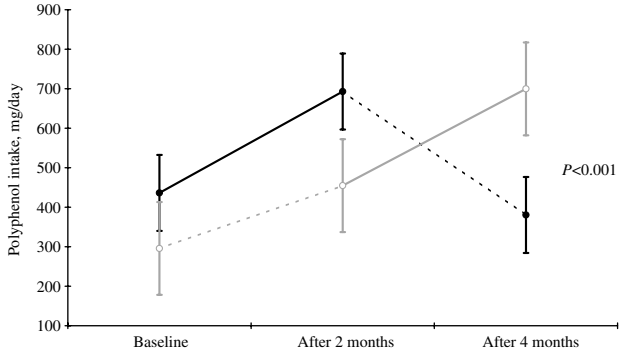

Figure 2 Changes in polyphenol intake in the Early (blacken circle) and Later (open circle) intervention groups. The straight line denotes the intervention period and the dotted line denotes the nonintervention period.

level, HOMA index, serum lipid level or high-sensitive C-reactive protein level associated with the intervention. There was no significant carryover effect of the hemoglobin A1c level or diastolic blood pressure levels, that is, a term for intervention received in the previous intervention period ($P>0.10$, not shown in the table).

Discussion

Among the subjects in this study, the mean baseline BMI was 25.4 in the Early intervention group and 26.0 in the Later intervention group. Over half of the subjects in each group were overweight. Furthermore, the mean systolic blood pressure was in the upper range of normal, and the mean diastolic blood pressure was in the borderline hypertensive range. The mean value of the HOMA index (Japan Diabetes Society, 2002), which is a marker of insulin resistance, was >3.0 and the proportion of subjects with HOMA index >2.5 was 71% in both groups, indicating that the majority of the subjects had insulin resistance (Kashiwabara *et al*., 2000; Japan Diabetes Society, 2002; Mclaughlin *et al*., 2003; McNeely *et al*., 2003).

The reason for the significant change appeared only in hemoglobin A1c was probably the stability for this measure, representing the average levels of serum glucose during the past 90 days. In our trial, the difference in polyphenol intake between the intervention and nonintervention periods was moderate because we allowed the subjects to consume green tea as usual. This could be another reason we did not see significant differences in fasting serum glucose, serum insulin levels or HOMA.

A previous trial for the 4-week supplement of a small amount of green tea (9 g per day) for 55 diabetes patients showed no effect on serum blood glucose levels (Ryu *et al*., 2006).

During the intervention period, the polyphenol intake was significantly increased by the intervention in the Early and Later intervention groups. The estimated polyphenol intake before and at the completion of the intervention was 441 mg (four cups of green tea) and 693 mg (seven cups of green tea), respectively, in the Early intervention group, while it was 466 mg (four cups of green tea) and 700 mg (seven cups of green tea), respectively, in the Later intervention group. Thus, our result suggests that an increase of polyphenols

Table 3 Changes in constitutional and biochemical markers of the Early and Later intervention groups

	Baseline	*After 2 months*	*After 4 months*	P
Main outcome measures				
Hemoglobin A_{1c} (%)				
Early intervention	6.2±2.0	5.9±1.9	5.8±1.7	0.03
Later intervention	6.1±1.3	6.1±1.4	5.9±1.4	—
Fasting serum glucose (mmol/l)				
Early intervention	7.5±3.5	7.0±2.7	6.7±2.1	0.18
Later intervention	7.7±2.5	7.2±1.6	7.2±2.0	—
Fasting serum insulin (μU/ml)				
Early intervention	8.8±7.3	7.4±7.3	8.7±14.7	0.41
Later intervention	10.3±10.1	6.5±4.0	6.1±3.0	—
HOMA				
Early intervention	3.0±2.9	2.4±2.5	2.8±5.5	0.35
Later intervention	3.7±4.4	2.1±1.3	2.0±1.2	—
Physiological measures				
Weight (kg)				
Early intervention	68.3±14.6	67.4±13.9	67.1±13.7	0.19
Later intervention	70.2±12.2	69.7±11.7	69.5±11.8	—
Body mass index (kg/m^2)				
Early intervention	25.4±5.0	25.1±4.8	24.9±4.5	0.14
Later intervention	26.0±4.1	25.8±4.1	24.9±6.2	—
Body fat (%)				
Early intervention	28.0±10.1	27.2±7.4	25.0±6.6	0.45
Later intervention	28.1±6.5	27.1±6.6	25.6±6.2	—
Systolic blood pressure (mm Hg)				
Early intervention	137.9±14.8	129.8±19.9	127.9±19.4	0.43
Later intervention	137.6±17.5	129.0±17.0	127.4±18.8	—
Diastolic blood pressure (mm Hg)				
Early intervention	91.7±10.5	81.9±15.0	83.2±10.7	0.06
Later intervention	87.0±11.0	83.4±12.5	83.6±10.9	—
Other biochemical measures				
Triglyceride (mg/dl)				
Early intervention	154.2±111.3	185.2±320.3	139.9±97.0	0.27
Later intervention	151.3±89.2	153.8±85.7	156.6±104.8	—
Total cholesterol (mg/dl)				
Early intervention	224.8±38.6	213.3±43.8	210.3±32.8	0.26
Later intervention	220.1±33.8	212.4±29.1	206.3±30.2	—
HDL cholesterol (mg/dl)				
Early intervention	57.3±10.1	55.5±10.5	53.5±9.6	0.2
Later intervention	54.3±14.9	54.1±14.2	51.2±12.0	—
LDL cholesterol (mg/dl)				
Early intervention	136.7±33.6	129.7±33.5	128.9±28.2	0.45
Later intervention	135.6±31.5	127.5±29.3	123.8±31.5	—
C-reactive protein (μg/dl)				
Early intervention	110±109	131±200	162±429	0.15
Later intervention	123±163	67±52	132±164	—

Abbreviations: HOMA, homeostasis model assessment; HDL, high-density lipoprotein; LDL, low-density lipoprotein.
Values are expressed as mean±s.d.

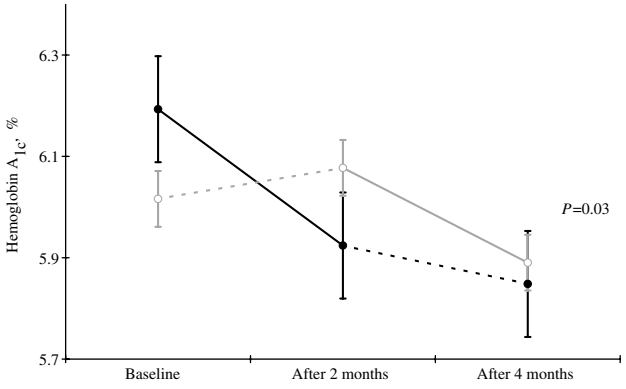

Figure 3 Changes in hemoglobin A1c levels in the Early (blacken circle) and Later (open circle) intervention groups. The straight line denotes the intervention period and the dotted line denotes the nonintervention period.

intake by 250–300 mg per day by supplementation corresponded to the intake of three cups of green tea, which may contribute to lowering of hemoglobin A1c levels.

A recent cohort study has shown that green tea consumption was inversely associated with risk of diabetes (Iso *et al.*, 2006) and the result supported our finding.

The intakes of major nutritional elements such as energy, proteins, lipids, carbohydrates and sodium chloride were comparable between the subjects in this study and those in the National Health and Nutrition Survey of Japan (Kenko Eiyo Joho Kenkyukai, 2005). In subjects with such nutritional status, the influence of additional intake of green tea on dietary habits was examined. We found that the intervention with green tea did not significantly affect the intake of nutritional elements except for sodium chloride, which significantly increased during the intervention in both the Early and Later intervention groups.

It was presumed that additional green tea intake leads to increased consumption of Japanese-style foods such as rice, miso soup, simmered food and pickles. Despite increased salt intake by the additional green tea intervention, there were few adverse effects in the present trial. The subjects consumed relatively abundant amounts of vegetables, fruits and other foods as well as green tea, which resulted in moderate to large intake of potassium, calcium and magnesium. For example, the decreasing tendency of the diastolic blood pressure by the intervention supports this speculation.

We did not find any effect of green tea-extracted powder supplementation on serum lipids, which was consistent with the results of previous trials (Princen *et al.*, 1998; Erba *et al.*, 2005).

The present study had several potential limitations. First, because of no washout period, a carryover effect could be occurred for the Early intervention group. The carryover effect in the present study, however, was small and statistically insignificant. Second, although approximately 80% of the subjects had a good compliance for green tea powder supplementation, they tended to reduce the usual intake of green tea, which made the differences in polyphenols intake between the intervention and nonintervention periods smaller than we expected.

Diabetes is considered to progress via a series of processes of insulin elevation by decreased sensitivity to insulin, and further reduction in insulin secretion (The Japan Diabetes Society, 2004). Animal experiments showed that intake of green tea polyphenol increased insulin activity (Richarda and Dolansky, 2002). Catechin suppressed glucose absorption in the small intestine, and the water extract of green tea had insulin-like activities and reduced the serum glucose level (Shimizu *et al.*, 1988; Shimizu, 2002). In addition, tea catechin elicited antidiabetic activities by suppressing gluconeogenic enzymes in a dose-dependent manner (Mary *et al.*, 2002). Caffeine, another constitute of green tea, increases basal energy expenditure and increased lipolysis from peripheral tissues (Astrup *et al.*, 1990) and oxidation/mobilization of glycogen in muscle (Spriet *et al.*, 1992).

The glycosylated hemoglobin is a marker of the average fasting serum glucose level during the past 1–2 months, and is considered to be useful for evaluating the status of glucose abnormality longitudinally (Nara, 2005). The HbA1c level was examined at baseline, 2 and 4 months in the Early and Later intervention groups in this crossover study, and the intervention of additional polyphenol intake had a significant effect on the HbA1c level ($P = 0.03$).

In conclusion, the randomized crossover trial demonstrated that 2-month supplementation of 544 mg polyphenol (456 mg catechin) per day improved glucose abnormality among individuals with borderline diabetes.

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