RESEARCH COMMUNICATION

Higher Consumption of Green Tea may Enhance Equol Production

Naoto Miyanaga[1], Hideyuki Akaza[1], Naomi Takashima[1], Yoshie Nagata[2], Tomoko Sonoda[2], Mitsuru Mori [2], Seiji Naito[3], Yoshihiko Hirao[4], Taiji Tsukamoto[5], Tomoaki Fujioka[6]

Abstract

Background: Our previous case-control study revealed that Japanese living in Japan and Koreans living in Korea can be divided into equol producers who have an ability to metabolize daidzein to equol and non-producers, and that the incidence of prostate cancer is higher in the latter group. In the present study, we examined relationships between type of food intake and the capacity for equol production in Japanese subjects.

Methods: The subjects were the individuals analyzed for the ability to produce equol in our previous study and newly registered cases. From December 2000 to December 2002, 276 hospitalized patients were interviewed face-to-face and blood samples were collected before breakfast. These included 122 patients with prostate cancer and 154 age-matched controls. Result: The frequency of equol producers (0.5 ng/ml or more) among cases and controls was 29% and 45%, respectively (p = 0.004). The consumption of soybeans and green tea were significantly higher in equol producers than in the non-producers (p<0.05). By contrast, the consumption of selenium and fiber was significantly lower in equol producers (p<0.05). Conclusion: Our results suggest that higher consumption of soybean and green tea are strongly related to the establishment of a capacity for equol production.

Key Words: isoflavones - prostate cancer - equol

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Introduction

The incidence of prostate cancer has been shown to be lower in Asian countries than in Europe and the United States (Parkin et al., 1997). Not a few investigators have reported that soybean isoflavones might have a significant role in the suppression of prostate cancer (Aklercreutz, 2002). Our previous case-control study (Akaza et al., 2002) revealed that Japanese living in Japan could be divided into those who are able to degrade daidzein, one of soybean isoflavones, to equol (equol producers) and those without this ability (equol non-producers), and that the incidence of prostate cancer is higher in the latter group.

As the mechanism, intestinal bacterial flora is supposed to metabolize daidzein into equol (Kelly et al., 1995). On the other hand, the type of foods consumed affects the intestinal bacterial flora (Xu et al., 1995). In the present study, we examined the relationship between the type of foods consumed and the ability of equol production.

Materials and Methods

Patients

The subjects are composed of the subjects that were analyzed for the ability of equol production in our previous study and new subjects registered afterwards. From December 2000 to December 2002, 276 hospitalized patients were interviewed face-to-face and their blood was collected before breakfast. These included 122 patients with prostate cancer and 154 age-matched controls.

[1]Department of Urology, Institute of Clinical Medicine, University of Tsukuba. [2]Department of Public Health, Sapporo Medical University School of Medicine. [3]Department of Urology, Faculty of Medicine, Kyushu University. [4]Department of Urology, Nara Medical School. [5]Department of Urology, Sapporo Medical University School of Medicine. [6]Department of Urology, Iwate Medical School.
For reprints and all correspondence: Hideyuki Akaza, M.D., Department of Urology, Post-graduate University of Tsukuba, 1-1-1, Ten-nodai, Tsukuba-shi, Ibaraki, 305-8575, Japan. E-mail: akazah@md.tsukuba.ac.jp

Patients having any other type of cancer were excluded from the controls, as were patients who were on a special diet or patients whose digestive and absorptive functions was impaired by the prostate cancer. The primary diagnoses of the controls were 112 ophthalmologic diseases such as cataracts, glaucoma or retinal detachment, 34 dental and oral diseases such as impacted teeth, osteomyelosis or mandibular cysts, 4 orthopedic diseases, 3 urogenital diseases, and 1 dermatologic disease. Informed written consent was given by all patients participating in the study.

Questionnaire

All patients were interviewed face-to-face using a semi-quantitative structured questionnaire. We surveyed the dietary and lifestyle variables for the year before diagnosis. The food questionnaire considered 102 foods and 4 beverages. Consumption of the following was compared between cases and controls: rice, meat, fish, eggs, milk, dairy products, all vegetables, green-yellow vegetables, fruits, all soy bean products, alcohol, coffee, black tea and green tea.

Blood Sample

The subjects of this study underwent the interview and blood sampling simultaneously. Blood was collected from patients before breakfast. The serum samples were stored at -20 °C until assay. Isoflavones (genistein, daidzein and equol) were analyzed by the LC-MSMS method (Akaza et al., 2002). The detection limit of the method was 0.5 ng/ml.

Statistical Analysis

Statistical analyses were performed using Wilcoxon's test (non-parametric) and the chi-square test. A p-value of <0.05 was defined as representing a statistically significant difference. The SAS JMP4.0 program was used as the statistical software.

Results

Blood Isoflavone Concentration (Table 1)

The median values of genistein and daidzein in all of the 276 subjects were 83.7 ng/ml and 24.1 ng/ml, respectively. An equol producer was defined as an individual with a detectable blood equol concentration (0.5 ng/ml or more). The frequency of equol producers among cases and controls was 29% (35/122) and 45% (70/154), respectively (p = 0.004).

The median age of all cases was 67 years old, and there was no age difference between the equol producers and non-producers. The median body mass index (BMI) in all cases was 23.5, and there was also no difference between equol producers and non-producers. The blood concentrations of genistein was higher in the equol producers than in the non-producers (p<0.05)π.

Food and Nutrient Consumption (Table 2, 3)

When the relationships of food intake and equol production are analyzed, the consumption of soybeans and green tea was significantly higher in the equol producers than in the non-producers (p<0.05). The consumption of yellow and green vegetables and fruits was greater in equol producers, and consumption of meat was greater in non-producers, but there was no statistical difference.

On the other hand, consumption of selenium and fiber was significantly lower in the equol producers than in the non-producers (p<0.05). The consumption of calories, protein and fat was higher in equol producers but without significant differences.

Discussion

We previously reported that equol non-producers were found more frequently in the prostate cancer group than in an age-matched control group (Akaza et al., 2002). However, clear explanation of the relationship between equol production and prostate has not yet been made. The stronger estrogenic action of equol among isoflavones may have protective effect against prostate cancer (Kelly et al., 1995), or the equol producer might have more important host factor other than estrogenic action of equol.

It has been reported that the metabolism of daidzein to equol is related to the intestinal bacterial flora (Kelly et al., 1995). The composition of the bacterial intestinal flora is influenced by dietary components. Healthy adult urban Canadians consuming a low-fiber and high-fat diet showed a greater percentage of Bacillus and Eubacterium species in the total bacterial population. In contrast, the dominant bacterial species in rural Japanese consuming high-fiber, low-fat diets consisted of Bifidobacteria and Eubacterium species (Rao, 1995).

About food consumption and equol production, Lampe et al. reported the results of intervention trial of 30 women consuming a western diet. The females in their study who

Table 1. Equol Production and Blood Isoflavone Concentration (n=276)

	Producers (n=105)	Non-producers (n=171)	p
Age	68	67	0.544
BMI	23.5	23.5	0.343
Genistein (ng/ml)	69.6	89.3	0.033
Daidzein (ng/ml)	19.8	26.9	0.305

Wilcoxon's test

*%(number) of prostate cancer patients among equol producers and non-producers.

Table 2. Equol Production and Foods Consumed (n=276)

Item	Equol production	N	Median	p*
Meat (g/day)	producer	105	34.2	
	non-producer	171	39.4	0.401
Vegetables (g/day)	producer	105	223.8	
	non-producer	171	228.5	0.284
Green and yellow vegetables (g/day)	producer	105	133.1	
	non-producer	171	109.7	0.174
Seafoods (g/day)	producer	105	68.9	
	non-producer	171	74.3	0.973
Eggs (g/day)	producer	105	36.1	
	non-producer	171	30.1	0.242
Dairy products (g/day)	producer	105	20.6	
	non-producer	171	20.9	0.842
Soybeans (g/day)	producer	105	128.2	
	non-producer	171	108.8	0.020**
Fruits (g/day)	producer	105	169	
	non-producer	171	144.5	0.437
Green tea (ml/day)	producer	105	450.0	
	non-producer	171	300.0	0.022**
Coffee (ml/day)	producer	105	64.1	
	non-producer	171	150.0	0.962
Black tea (ml/day)	producer	105	0.0	
	non-producer	171	0.0	0.211

*Wilcoxon's test
**p<0.05

Table 3. Equol Production and Nutrient Intake (n=276)

Item	Equol production	N	Median	p*
Total calories Kcal/day	producers	105	1712.2	
	non-producers	171	1765.6	0.740
Protein g/day	producers	105	68.3	
	non-producers	171	71.5	0.968
Fat g/day	producers	105	40.7	
	non-producers	171	41.6	0.721
Carbohydrate g/day	producers	105	243	
	non-producers	171	242.7	0.630
Na mg/day	producers	105	2557.4	
	non-producers	171	2633.9	0.869
K mg/day	producers	105	3054.1	
	non-producers	171	2880.1	0.646
Ca mg/day	producers	105	567.7	
	non-producers	171	507.5	0.220
Mg mg/day	producers	105	202.1	
	non-producers	171	198.5	0.478
Fe mg/day	producers	105	9.4	
	non-producers	171	9.5	0.282
Zn mg/day	producers	105	7.6	
	non-producers	171	8.6	0.080
Cu mg/day	producers	105	0.13	
	non-producers	171	0.16	0.577
Se µg/day	producers	105	76.7	
	non-producers	171	88.6	0.037**

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Table 3. Equol Production and Nutrient Intake (n=276) (Continue)

Item	Equol production	N	Median	p*
Retinol mg/day	producers	105	157.6	
	non-producers	171	161.3	0.819
Carotene mg/day	producers	105	2678.9	
	non-producers	171	2698.2	0.982
Vitamin A (mg/day)	producers	105	720.2	
	non-producers	171	750	0.934
Vitamin D (mg/day)	producers	105	8.9	
	non-producers	171	8.1	0.685
Vitamin E (mg/day)	producers	105	7.2	
	non-producers	171	6.8	0.323
Vitamin K (mg/day)	producers	105	255.1	
	non-producers	171	244	0.690
Vitamin B1 (mg/day)	producers	105	0.80	
	non-producers	171	0.79	0.813
Vitamin B2 (mg/day)	producers	105	1.41	
	non-producers	171	1.48	0.735
Niacin (mg/day)	producers	105	18	
	non-producers	171	18.2	0.654
Vitamin B6 (mg/day)	producers	105	0.92	
	non-producers	171	0.92	0.629
Vitamin B12 (mg/day)	producers	105	7.09	
	non-producers	171	7.43	0.908
Folic acid (mg/day)	producers	105	343.2	
	non-producers	171	320.2	0.243
Pantothenic acid (mg/day)	producers	105	6.54	
	non-producers	171	6.33	0.983
Vitamin C (mg/day)	producers	105	136.2	
	non-producers	171	125.5	0.259
Daidzein (mg/day)	producers	105	1.29	
	non-producers	171	1.15	0.156
Glycitein (mg/day)	producers	105	0.08	
	non-producers	171	0.10	0.206
Genistein (mg/day)	producers	105	1.38	
	non-producers	171	1.44	0.763
Isoflavone (mg/day)	producers	105	59.2	
	non-producers	171	47.0	0.166
Fiber (g/day)	producers	105	15.5	
	non-producers	171	19.6	0.004**

*Wilcoxon's test
**p<0.05

excreted equol in urine had a significantly higher intake of dietary fiber and a lower fat-to-fiber ratio than the non-producers (Lampe et al., 1998). Rowland et al. reported that 36% of individuals in an intervention trial were equol excreters and that their nutritional intake had a low lipid energy ratio and a significantly high carbohydrate energy ratio (Rowland et al., 2000).

In the present study, the consumption of soybeans and green tea was significantly higher in equol producers than in non-producers. It is suggested that the dietary consumption of soybean and green tea increase the capacity of gut microbial flora to synthesize equol.

Epidemiologically, in our case-controlled study of prostate cancer and food consumption (Nagata et al., 2002), a trend was observed for an increase in the amount of green tea drunk per day to reduce the risk of prostate cancer. A main component of green tea, epigallocatechin gallate (EGCG), has been reported to suppress the promotion of cancer in in vitro and in vivo experiments (Fujiki et al., 2002), however, the other anti-anaplastic mechanism may exist.

In conclusion, further examination is necessary to confirm that green tea and other dietary components promote the growth and/or activity and/or arrangement of the bacterial populations responsible for equol production. Whether increasing green tea consumption changes the species composition of the microflora and/or bacterial activities remains controversial. If the control of equol production is possible, the prevention of sex hormone-related cancer such as prostate cancer is expected in the future.

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