

A Prospective Study on Ginseng Intake and Cancer for Population — Preliminary Report —

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Abstract □ We conducted a prospective cohort study to evaluate the preventive effect of ginseng on the development of cancer in the population over 40 years old residing in Kangwha-eup from August 1987 to December 1992. Among 4,634 persons (2,362 men, 2,272 women), 335 (7.6%) persons had died. Cancer accounted for 79 (22.8%) of the total death. Of 4,634 persons eligible for analysis, 70.4% (3,263) were ginseng intakers. Ginseng intakers had a decreased risk (RR=0.48, 95% CI: 0.34~0.67) compared with non-intakers. The relative risk of cancer according to the kind of ginseng was 0.23 (95% CI: 0.08~0.63) for fresh ginseng extract intakers. There was a decrease in risk with rising the frequency of ginseng intake, showing statistically significant dose-response relationship. The longer the duration of ginseng intake or the greater the total number of ginseng consumed, the lower the risk. Newly diagnosed cancer cases have been identified: 42 stomach, 24 lung, 14 liver and 57 at other sites. The relative risks of ginseng intakers were 0.34 (95% CI: 0.19~0.60) in gastric cancer and 0.27 (95% CI: 0.12~0.60) in lung cancer. Among ginseng preparations, fresh ginseng intakers were significantly associated with the decreased risk of gastric cancer (RR=0.19, 95% CI: 0.04~0.98). These results strongly revealed that *Panax ginseng* C.A. Meyer (Korean ginseng) has preventive effect against cancer.

Key words □ Prospective study, intake of ginseng, cancer, cohort study.

Introduction

Ginseng has been used as one of the most valuable natural tonics in the Orient over 2,000 years. For many centuries, especially, Korean ginseng has been known as the 'elixir of life', a mysterious herbal medicine widely used for the prevention and cure of various ailments.¹⁾ It has been cultivated for more than one thousand years in the land between 33 to 42 degrees of the latitude which is very suitable for the cultivation. In 1843, C.A. Meyer, a Russian scientist, gave Korean ginseng the name *Panax ginseng* to set it apart from the other ginseng species, *Panax japonicum* of Japan, *Panax notoginseng* of China and *Panax quinquefolium* of the USA and Canada.²⁾ In Korea, Kangwha, Keumsan and Punggi areas are the suited locations for ginseng

production.

Although numerous studies have been reported that ginseng has various pharmacological activities, its efficacy is still unclear. Shennong of China in the sixth century described that the long-term consumption of ginseng could be ascribed to increase in the length of life.³⁾ In the previous animal experiment performed on the hypothesis that life prolongation effect of ginseng described by Shennong may be due to the preventive activity of ginseng against the development of cancers, we have observed the anticarcinogenic effect of red ginseng.⁴⁻¹⁰⁾ We also presented the data on the effect of ginseng intake in case-control studies of 1990¹¹⁾ and 1995.¹²⁾

The aim of the prospective study is to investigate whether ginseng intake is related to the mortality and morbidity of various cancers and to evaluate the preventive effect of ginseng in the population residing in ginseng production areas on the basis

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of the result of our previous case-control study.

Population and Methods

The study population was selected from persons who were listed in the 1987 resident's list registered in the provincial government of ginseng production areas. A cohort of 14,651 persons over 40 years age, residing in ginseng production areas (Kangwha-eup; 4,634, Punggi-eup; 2,952, Keum-san-eup; 2,044, Muju-eup; 3,367) and a comparison area (Keumchon-eup; 1,654) was interviewed and examined between August 1987 and December 1989 in order to investigate the preventive effect of ginseng on cancer.

Each study subject was interviewed by means of a standard questionnaire about demographic characteristics, life-long occupation, smoking and drinking habits, the past history of diseases, etc. In an attempt to obtain the detailed information about ginseng intake, we asked to specify their age of initial intake, and their frequency and duration of intake of ginseng.

Among areas studied, population in Kangwha-eup were followed-up for about five years. Newly diagnosed cases of cancer were identified by the continual surveillance of medical records of the related hospitals, death certificates of the provincial government, incidence data of Medical Insurance Cooperation, etc. A cohort member was classified as a cancer case if they had any disease code of cancer (International Classification of Diseases for Oncology 140-199) in the hospital records or death certificates.¹³⁾ Total number of subjects interviewed was 4,675. Among them 41 prevalence cancer cases were excluded. This left 4,634 study eligible subjects (2,362 men and 2,272 women) for analysis. During the surveillance period, 7.7% (355 of 4,634) of the subjects died, cancer accounting for 22.3% (79) of the total death (Table 2). The number of the dead due to senility and cardiovascular disease was 99 (27.9%) and 57 (16.1%), respectively. 47 patients (1.0%) with unknown diseases were excluded. This left 4,587 study eligible subjects for relative risk analysis.

The Mantel-Haenszel procedure¹⁴⁾ was used to

estimate the relative risk (RR) and 95% confidence interval (CI) of ginseng intake, adjusted by age and sex. The possibility of a linear trend in risk across exposure categories was tested by a trend statistic.

Results

The distribution of demographic and social cha-

Table 1. Percent distribution of demographic and social characteristics for subjects

Variables	Male	Female	Total
No. of studied population	2,362	2,272	4,634
Age group			
40~49	39.4	31.3	35.4
50~59	32.0	31.2	31.6
60~69	18.6	21.2	19.9
70~79	8.7	11.3	10.0
80~	1.3	5.0	3.1
Mean age (years)	54.2	56.9	55.5
Marital status			
Married	90.0	68.8	79.6
Widowed	7.5	29.0	18.1
Others	2.5	2.2	2.3
Religion			
None	45.8	39.8	42.8
Buddhism	24.3	27.7	26.0
Protestant	17.9	19.4	18.6
Catholic	5.5	6.3	5.9
Confucianism	5.1	4.7	4.9
Others	1.4	2.1	1.8
Education			
None	15.1	38.9	26.8
Primary school	38.6	45.1	41.8
Middle school	23.7	12.2	18.0
High school	19.0	3.3	11.3
College and above	3.6	0.5	2.1
Occupation			
Professional and technical workers	2.8	0.2	1.5
Administrative workers	0.2	0.1	0.1
Clerical workers	6.2	0.4	3.4
Service workers	6.6	1.2	4.0
Sales workers	18.3	11.9	15.2
Agricultural workers	37.2	27.9	32.6
Production workers and labourer	5.1	2.3	3.7
No occupation	23.6	56.0	39.5

Table 2. Distribution of confirmed cases for cancer and other diseases

Disease	No. of alived	No. of death	Total
All cancers	58	79(22.3)	137 (33.2)
Oral cavity and pharynx	1	1	2
Esophagus	1	2	3
Stomach	20	22	42
Colon	—	1	1
Rectum	4	2	6
Liver	4	10	14
Pancreas	—	3	3
Larynx	—	4	4
Lung	4	20	24
Leukemia	2	2	4
Female breast	8	1	9
Cervix uteri	2	2	4
Ovary	1	—	1
Urinary bladder	1	1	2
Thyroid gland	1	—	1
Malignant lymphoma	5	1	6
Other cancers	4	7	11
Other diseases	—	229(64.5)	229(55.4)
Unknown	—	47(13.2)	47(11.4)
Total	58	355(100.0)	413(100.0)

Values in parenthesis indicate percent.

Table 3. Distribution of ginseng intake by subjects

Intake of ginseng	Male	Female	Total
Studied population	2,362 (100.0)	2,272 (100.0)	4,634 (100.0)
No intake of ginseng	578 (24.5)	789 (34.7)	1,367 (29.5)
Intake of ginseng	1,784 (75.5)	1,483 (65.3)	3,267 (70.5)
Fresh ginseng	139 (5.9)	108 (4.8)	247 (5.3)
Fresh ginseng extract	150 (6.4)	156 (6.9)	306 (6.6)
White ginseng extract	33 (1.4)	37 (1.6)	70 (1.5)
White ginseng powder	94 (4.0)	58 (2.6)	152 (3.3)
Red ginseng	15 (0.6)	9 (0.4)	24 (0.5)
Ginseng tea	282 (11.9)	182 (8.0)	464 (10.0)
Boiled chicken with young ginseng root	177 (7.5)	220 (9.7)	397 (8.6)
Fresh ginseng and fresh ginseng extract	42 (1.8)	40 (1.9)	82 (1.8)
Fresh ginseng and white ginseng extract	57 (2.4)	34 (1.5)	91 (2.0)
Fresh ginseng and white ginseng power	40 (1.7)	31 (1.4)	71 (1.5)
Fresh ginseng and ginseng tea	217 (9.2)	136 (6.0)	353 (7.6)
Fresh ginseng and red ginseng	9 (0.4)	12 (0.6)	21 (0.5)
Fresh ginseng extract and white ginseng extract	7 (0.3)	10 (0.4)	17 (0.4)
Fresh ginseng extract and white ginseng power	33 (1.4)	17 (0.7)	50 (1.1)
Fresh ginseng extract and red ginseng	2 (0.1)	5 (0.2)	7 (0.2)
White ginseng extract and white ginseng power	6 (0.3)	4 (0.2)	10 (0.2)
White ginseng power and red ginseng	3 (0.1)	3 (0.1)	6 (0.1)
Others	478 (20.1)	421 (18.3)	899 (19.3)

Values in parenthesis indicate percent.

characteristics for subjects residing in Kangwha-eup was shown in Table 1. The average age at interview was 54.2 for male and 56.9 for female. Buddhism was the most common religion. Females generally had fewer years of schooling, were more often widowed, and were from lower socioeconomic groups than males.

Of 4,634 persons eligible for analysis, 70.4% (3,267) was ginseng consumers (Table 3). Ginseng intakers had a decreased risk (RR=0.48, 95% CI: 0.34~0.67) for cancer compared with non-intakers (Table 4). On the type of ginseng, the RR of cancer was 0.23 (95% CI: 0.08~0.63) for fresh ginseng extract intakers. The RR for other types of ginseng showed a decreasing trend, but it was not statistically significant.

There was a decrease in risk with rising frequency of ginseng consumed, showing statistically significant dose-response relationship (Table 5). The RR ranged from 0.54 of those who had consumed for less than 3 times per year to 0.41 for those who had consumed for more than one time per month. For the duration of ginseng intakers, the

Table 4. Relative risks of cancer by ginseng intake

Kind of ginseng	Number of subjects	Number of cancer	RR	95% CI	Adjusted RR	95% CI
No intake	1,283	62	1.00	—	1.00	—
Ginseng intake	3,167	75	0.50	0.36~0.70	0.48	0.34~0.67
Fresh ginseng	236	8	0.71	0.35~1.46	0.66	0.32~1.39
Fresh ginseng extract	296	3	0.22	0.08~0.61	0.23	0.08~0.63
White ginseng powder	147	4	0.56	0.22~1.53	0.59	0.22~1.62
White ginseng extract	68	1	0.62	0.16~2.42	0.62	0.15~2.53
Red ginseng	24	—	—	—	—	—
			(0.43)	(0.03~6.77)	(1.81)	(0.48~6.88)
Boiled chicken with young ginseng root	381	12	0.66	0.36~1.21	0.77	0.40~1.23
Ginseng tea	442	18	0.85	0.51~1.42	0.89	0.52~1.52
Multiple combinations	1,573	28	0.38	0.25~0.58	0.37	0.24~0.57

Adjusted for age and sex.

RR=relative risk, CI=confidence interval.

Table 5. Relative risks of cancer by ginseng intake

Times of ginseng intake	Number of noncases	Number of cancer	RR	95% CO	Adjusted RR	95% CI
No intake	1,283	62	1.00	—	1.00	—
Frequency of ginseng intake						
1~3 times/year	1,439	39	0.57	0.39~0.85	0.54	0.36~0.82
4~11 times/year	924	21	0.48	0.30~0.77	0.49	0.30~0.79
1 time/month or more	804	15	0.40	0.23~0.68	0.41	0.24~0.71
Duration of ginseng intake						
1~ 4 years	2,073	45	0.46	0.32~0.67	0.44	0.30~0.65
5~ 9 years	656	18	0.58	0.35~0.96	0.59	0.35~0.97
10~19 years	336	7	0.44	0.21~0.93	0.44	0.21~0.94
Total times of ginseng intake for life-long (times)						
1~ 50	1,589	34	0.46	0.30~0.68	0.44	0.29~0.67
51~100	511	14	0.58	0.33~1.01	0.63	0.36~1.11
101~200	346	15	0.90	0.52~1.56	0.91	0.52~1.58
201~300	202	4	0.42	0.16~0.98	0.40	0.15~0.97
301~500	253	3	0.26	0.09~0.73	0.24	0.08~0.73
501~	266	5	0.40	0.17~0.95	0.38	0.15~0.95

Adjusted for age and sex.

RR=relative risk, CI=confidence interval

RR ranged from 0.59 for intakers of less than 9 years to 0.44 for intakers of more than 10 years. The RR of total life-time frequencies of ginseng intake ranged from 0.63 for intakers of less than 100 times to 0.38 for intakers of more than 500 times. The longer the duration of ginseng intake or the greater the total number of ginseng consumed, the lower the risk.

During the study period, 137 cancer cases have newly diagnosed as cancers including 42 stomach,

24 lung, 14 liver and 57 at other sites (Table 2). The RRs of ginseng intakers were 0.34 (95% CI: 0.19~0.60) in gastric cancer and 0.27 (95% CI: 0.12~0.60) in lung cancer, showing statistically significant (Table 6). Among ginseng preparations, only fresh ginseng extract intakers was associated with the decreased risk of gastric cancer (RR=0.19, 95% CI: 0.04~0.98), but other types of ginseng showed a decreasing trend.

Table 6. Adjusted relative risks and 95 confidence interval for selected cancer by ginseng intake

Ginseng intake	Number of subjects	Stomach (42)			Lung (24)			Liver (14)		
		No.	RR*	95% CI	No.	RR*	95% CI	No.	RR*	95% CI
No intake	1,283	23	1.00	—	14	1.00	—	4	1.00	—
Ginseng intake	3,167	19	0.34	0.19~0.60	10	0.27	0.12~0.60	10	0.94	0.27~3.27
Fresh ginseng	236	2	0.43	0.11~1.74	1	0.35	0.05~2.55	2	2.69	0.53~13.71
Fresh ginseng extract	296	1	0.19	0.04~0.98	1	0.32	0.05~2.09	—	—	—
White ginseng powder	147	1	0.38	0.06~2.40	—	—	—	—	—	—
White ginseng extract	68	2	1.62	0.39~6.71	—	—	—	—	—	—
Boiled chicken with young ginseng root	381	5	0.81	0.31~2.11	1	0.30	0.05~1.86	1	0.99	0.09~10.80
Ginseng tea	442	6	0.76	0.32~1.85	4	0.92	0.29~2.93	2	1.39	0.18~10.67

*Adjusted for age and sex.

Values in parenthesis indicate number of cancer.

RR=relative risk, CI=confidence interval.

Discussion

Animal experiments were performed on the hypothesis that the increase in the length of life of ginseng described by Shennong³⁾ may be due to the preventive effect of ginseng against the development of cancers. We reported that red ginseng had effects on pulmonary adenomas induced by 9,10-dimethyl-1,2-benzanthracene (DMBA), urethan, N-2-fluorenylacetamide (FAA), aflatoxin B₁ and benzo(a)pyrene (BP) in mice.^{4,5)} The administration of benzo(a)pyrene combined with fresh ginseng, however, did not decrease the incidence.⁶⁻⁸⁾

In February 1987, a case-control study was carried out on 905 cases admitted to Korea Cancer Center Hospital in order to investigate the preventive effect against cancer.¹¹⁾ The ginseng intakers had the odds ratio (OR) of 0.56 (95% CI: 0.46~0.69) for cancer compared with nonintakers. There was a decrease in risk with rising the frequency and duration of ginseng intake. We also extended the study subjects to evaluate ① the type of ginseng products that has the most prominent cancer preventive effect, ② the difference of preventive effect by sex, ③ the dose-response relationship by ginseng intake and ④ the type of cancer which can be prevented by ginseng.¹²⁾ As a results, the OR for cancer was 0.50 (0.44 in male and 0.54 in female) for ginseng intakers. On the type of ginseng, the ORs were 0.37 (95% CI=0.29~0.46) for fresh ginseng extract intakers, 0.57 (95% CI=0.48~0.68)

for white ginseng extract intakers, 0.30 (95% CI=0.22~0.41) and 0.20 (95% CI=0.08~0.50) for red ginseng intakers, respectively. The risks for cancer were lowered with increasing the frequency and duration of ginseng intake. Of the site of cancer, the ORs were 0.47 for cancer of the lip, oral cavity and pharynx, 0.20 for esophageal cancer, 0.36 for gastric cancer, 0.42 colorectal cancer, 0.48 for liver cancer, 0.22 for pancreatic cancer, 0.18 for laryngeal cancer, 0.55 for lung cancer and 0.15 for ovarian cancer. However, there was inconsistent and weak associations between ginseng intake and cancer of the female breast and uterine cervix.

In August 1987, a cohort study was carried out on the population residing in ginseng production areas to confirm ginseng effects on cancer after 6 months later of the case-control study. In Kangwha-eup, among 4,634 persons over 40 years of age, 7.7% (355) died. Cancer accounted for 22.3% (79) of the total death. Excluding 47 unknown disease cases, 54.7% of 137 cancer cases had a history of ginseng intake in comparison with 71.2% of 4,450 noncases. This showed a similar results in comparison with that of the proportion (78.1%) of control groups in the previous case-control studies.^{11,12)} The present study found a significant RR (0.48) between the intake of ginseng and cancer, as shown in the previous study (OR=0.51). On the type of ginseng, the RR of cancer was 0.23 (95% CI: 0.08~0.63) for fresh ginseng extract intakers and 0.37 (95% CI: 0.24~0.57) for multiple combination intakers. The

RRs for other types of ginseng showed a decreasing trend, but it was not statistically significant. The small number of red ginseng intakers made it difficult to evaluate the effect of ginseng though the previous study showed a decreasing OR. This study did not show any relationship between fresh ginseng intakers and cancer, being consistent in the experimental study⁶⁾ and the case-control study.^{11, 12)} On site, the RRs of ginseng intakers were 0.34 (95% CI : 0.19~0.60) in gastric cancer and 0.27 (95% CI : 0.12~0.60) in lung cancer. Among ginseng preparations, fresh ginseng intakers were significantly associated with the decreased risk of gastric cancer (RR=0.19, 95% : 0.04~0.98). In assessing the result of the case-control study, we consider the likely effect of ginseng on other cancers except cancer of the female breast and uterine cervix.

In conclusion, these results strongly revealed that *Panax ginseng* C.A. Meyer has preventive effect against cancer, providing support for the previous case-control studies.

요 약

본 연구는 인삼의 암발생 예방효과를 평가하기 위하여 국내 주요인삼생산지인 강화읍에 거주하는 40세 이상 주민을 대상으로 전향적 역학적 연구를 수행하였다. 총 참여자 4,634명 중 남성이 2,362명 그리고 여성이 2,272명이었으며, 그 중 335명(7.6%)이 사망하였다. 암사망자수는 79명으로 22.8%이었으며, 암발생환자는 58명이었다. 즉 총 암발생수는 137명(33.2%)이었다. 분석이 가능하였던 4,634명 중 3,263명(70.5%)이 인삼을 복용했다. 인삼복용자는 비복용자에 비하여 암발생위험도(RR)가 감소하여 0.48[95% 신뢰구간(CI) : 0.34~0.67]를 보였다. 인삼 종류별로 보면 수삼열탕복용자가 암에 이환될 위험도가 0.23[95% 신뢰구간(CI) : 0.08~0.63]이었다. 인삼복용빈도가 높을수록 위험도(RR)는 역으로 감소하는 현저한 양-반응관계를 보였다. 인삼복용기간이 길던가 복용빈도가 높을수록 위험도는 낮았다. 암의 종류별로 보면 위암이 42, 폐암이 14, 그리고 기타 암이 57명이었다. 위암의 위험도(RR)는 0.34[95% 신뢰구간(CI) : 0.19~0.60]이었고,

폐암은 0.27[95% 신뢰구간(CI) : 0.12~0.60]이었다. 본 연구의 결과는 증례-대조군 연구결과와 일치되며, 고려인삼의 복용으로 암이 예방됨을 입증하였다.

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