Assessment of Preference for Breast Cancer Chemoprevention in Japanese Young Women

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Pills containing estrogen and progesterone or gonadotropin releasing hormone agonist have been considered valuable to prevent breast cancer. This study assessed preference for the combination-type pill for preventing breast cancer, to evaluate the hypothetical preventive effect of this agent among young Japanese women. The standard gamble method was applied. Fifty-five college students and 44 nursing school students aged between 18 and 41 years were asked to decide the probability of being affected by breast cancer at which they would start to take this agent. Preference score was calculated by subtracting the probability given by each respondent from 1, which corresponds to the value (utility) she allotted to the agent. The means of preference score were 0.58, 0.48, 0.37, and 0.27 for 100, 75, 50, and 25% of efficacy levels of the agent, respectively. Preference score was significantly lower in nursing school students and those whose knowledge about hormones were relatively high. Score of Health Locus of Control (HLC) was nonsignificantly negatively correlated with preference score at any efficacy level. HLC score was significantly higher among those who refused the agent with 50 and 25% efficacy levels at 100% level of breast cancer risk. The data suggest that perceived risk of this agent was not negligibly small in this population and school status, knowledge about hormones, and beliefs about health would affect preference for the agent. Understanding of preference for chemopreventive agents for breast cancer, especially those containing hormones, is important to assess their potential as future preventive agents and is helpful when planning a strategy of chemoprevention.

Key words: Breast cancer — Preference — Hormones — Health locus of control — Chemo-prevention

In recent years, breast cancer has been an important public health problem facing women in Japan. According to data from the Miyagi Cancer Registry, breast cancer incidence rate rose more than two-fold between the periods of 1959–1961 and 1983–1987.[1, 2] Primary prevention for this disease is likely to be an important issue in Japan in the near future.

Prevention can be achieved by altering risk factors of breast cancer. However, the recognized risk factors of breast cancer, such as age at menarche, age at first birth, and age at menopause are not readily changeable through either behavioral or environmental modifications. The use of drugs to prevent breast cancer has become of interest in the U.S., where breast cancer incidence is high.[3] Hormones are the key to promotion of the carcinogenetic process of breast tissue.[4] Synthetic hormone-like agents, such as tamoxifen and ralorifene, and pills containing estrogen and progesterone or gonadotropin releasing hormone agonist have been considered valuable to prevent breast cancer because they block the effect of estrogen.[3, 5] Trials assessing the potential risks and benefits of some of these agents are under way among women at high risk of breast cancer.[6, 7] Strategically, earlier intervention should have a better general effect on the population. Chemopreventive agents could have a beneficial reducing effect of cancer incidence, if employed widely among young women.[5]

The concept of controlling estrogen exposure by using pharmacological methods is not familiar to the general public in Japan. The feasibility (benefits and risks) of these agents for chemoprevention has not been established yet. There may be reluctance to support the use of these agents because people feel they are unnatural or are concerned about adverse effects. Using a example of combination-type pill, I assessed preference for this agent among young Japanese women in settings where information about hypothetical effects of the agent on breast cancer prevention was provided. I also examined whether preference for this agent is associated with present and past health histories, knowledge about hormones, Health Locus of Control (HLC),[8] and other lifestyle variables.

MATERIALS AND METHODS

Fifty-five college students and 44 students at a nursing school participated in the present study. No women refused to enter the study. Subjects were given a sheet containing the following information on hormonal chemoprevention: "It is acknowledged that sex hormones play a large part in determining breast cancer risk. A hormonal agent controlling hormones is considered to prevent breast cancer. A clinical trial using this agent is under way among women at high risk of breast cancer in the U.S., where the breast cancer incidence is high."

To measure the preference for chemoprevention using this agent, I utilized the standard gamble method.[9] The following hypothetical outcome was presented: "If you take this agent, you are free of breast cancer with a probability of 100%."

Subjects were asked to decide the probability of being affected by breast cancer at which they would start to take this agent. I did not provide further information on possible side effects of this agent and asked them to make their decision based on the information I gave above and their own ideas. I assessed preference for this agent at various hypothetical levels of efficacy of the agent, i.e., 100, 75, 50, and 25% probability of being free of breast cancer. Each subject was asked whether they understood the questions and any necessary explanation was given in a personal interview. Data on present perceived health status, demographic characteristics, present and past disease histories, smoking status, reproductive history, frequency of visits to physicians, medication use, and history of cancer among first and second-degree relatives was obtained by a self-administered questionnaire. Level of knowledge about hormones (high, moderate, low, and very low) was based on self-assessment of the subjects. HLC scale (Wallston, Wallston, Kaplan & Maides, 1976) was used to measure internal or external control. HLC refers to the beliefs people have about who or what determines their health status. People who believe that their own behavior (forces that they control) determines whether they stay healthy are considered to have internal HLC orientation. People who believe that forces outside their control are critical are considered to have an external HLC orientation.[8]

Preference score for this agent in the jth scenario, denoted by Z_j, was given by

$$Z_j = 1 - q_j,$$

where q_j is the probability being affected by breast cancer when the respondent starts to take the agent in the jth scenario. If the agent was rejected at 100% level of breast cancer risk, value 0 was given to the preference score. Associations of preference score with categorical study variables were examined using analysis of variance. Spearman correlation coefficients were calculated to assess the relationship between preference score and HLC score. The means of HLC score were compared between those who refused the agent at 100% breast cancer risk and the rest.

RESULTS

The means (SD) of age were 19.3 (0.47) for college students and 24.6 (5.3) for nursing school students. One college student and 7 nursing school students were married. About half of the entire students (55.1%, i.e.,

Table I. Distribution of Preference Score for Breast Cancer Preventive Agent According to Its Hypothetical Efficacy Level

Preference score	Efficacy level (%)			
	100	75	50	20
	n (%)	n (%)	n (%)	n (%)
0	15 (15.2)	22 (22.2)	30 (30.3)	40 (40.8)
0.01–0.19	2 (2.0)	5 (5.1)	6 (6.1)	8 (8.1)
0.2–0.39	9 (9.1)	12 (12.1)	15 (15.2)	20 (20.3)
0.4–0.59	21 (21.0)	15 (15.2)	23 (23.2)	15 (15.3)
0.6–0.79	13 (13.1)	23 (23.2)	8 (8.0)	0 (0.0)
0.8–0.99	38 (38.4)	22 (22.2)	17 (17.1)	15 (15.3)
1.0	1 (1.0)	0 (0.0)	0 (0.0)	0 (0.0)

Table II. Preference Score (mean and SD) in College and Nursing School Students for Breast Cancer Preventive Agent According to Its Hypothetical Efficacy Level

Efficacy level (%)	College students (n = 55)	Nursing school students (n = 44)	College & Nursing school students (n = 99)
100	0.71 (0.31)	0.43 (0.34)**	0.58 (0.35)
75	0.60 (0.32)	0.32 (0.34)**	0.48 (0.35)
50	0.48 (0.33)	0.24 (0.32)**	0.37 (0.35)
25	0.28 (0.34)	0.16 (0.30)**	0.23 (0.34)

** $P < 0.01$ for difference in the scores between college and nursing school students.

48.2% of college students and 51.7% of nursing school students) perceived that they were as healthy as others of their age. No one reported herself to be in poor health. The mean (SD) numbers of visits to physician during the previous year was 2.1 (4.7) for college students and 2.5 (7.9) for nursing students.

The distribution of preference score is presented in Table I. The mean of preference scores for the agent was 0.58 even when it hypothetically prevented breast cancer completely (Table II). One college student and 6 nursing school students consistently rejected the agent even when they were at 100% level of breast cancer risk.

Preference score was significantly lower in nursing school students than in college students at any efficacy level of the agent (Table II). Those who rejected the agent at 100% level of breast cancer risk were more likely to be nursing school students (Table III).

No one reported herself to have good knowledge about hormones. Preference score was significantly negatively associated with level of knowledge about hormones (Table IV). The reported knowledge level about hormones was higher in nursing school students than in college students (the proportions of those who reported moderate, low, and very low knowledge levels were 29.6,

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Table III. Number (%) of Subjects Who Rejected the Breast Cancer Preventive Agent at 100% Level of Breast Cancer Risk According to Hypothetical Efficacy Level of the Agent and School Status

Efficacy level (%)	College students (n=55)	Nursing school students (n=44)	College & Nursing school students (n=99)
100	1 (1.8)	6 (13.6)*	7 (7.0)
75	1 (1.8)	16 (36.4)**	17 (17.1)
50	3 (5.5)	21 (47.7)**	24 (24.2)
25	7 (12.7)	27 (49.1)**	34 (34.3)

* P<0.05 for comparison between college and nursing school students.
** P<0.01 for comparison between college and nursing school students.

Table IV. Preference Score (mean and SD) for Breast Cancer Preventive Agent According to Levels of Hypothetical Efficacy of the Agent and Knowledge about Hormones

Efficacy level (%)	Knowledge level[a]		
	Very low (n=17)	Low (n=67)	Moderate (n=15)
100	0.82 (0.26)	0.59 (0.33)	0.27 (0.28)**
70	0.71 (0.30)	0.48 (0.34)	0.20 (0.27)**
50	0.62 (0.33)	0.36 (0.33)	0.15 (0.23)**
25	0.48 (0.40)	0.27 (0.33)	0.10 (0.19)**

a) No women reported a high level of knowledge.
** P for F value <0.01.

Table V. Relationships of Health Locus of Control (HLC) Score to Preference for the Breast Cancer Preventive Agent According to Its Hypothetical Efficacy Level

Efficacy level (%)	Correlation[a] of HLC with preference scores	Age-adjusted HLC score[b]	
		Refusers	Non-refusers
100	−0.07	27.1 (1.7)	27.9 (0.5)
75	−0.12	29.5 (1.1)	27.5 (0.5)
50	−0.12	29.5 (1.0)	27.4 (0.6)*
25	−0.15	29.2 (0.9)	27.1 (0.6)*

a) Spearman correlation coefficients after controlling for age.
b) Mean (SE).
* P<0.05.

the agent with 50% efficacy level at 100% level of breast cancer risk.

Age, past history of endocrinological diseases, hospitalization, and operation, family history of cancer, smoking status, marital status, and parity were not related to preference score or to refusal of the agent at 100% level of breast cancer risk. No one reported hearing previously about the trial of combination type pills as chemopreventive agents.

DISCUSSION

It is important to understand preference for potential chemopreventive agents to get an idea of the feasibility of their use in the future. I quantitatively assessed preference for a chemopreventive agent containing hormones, since I anticipated that women might be reluctant to use hormonal agents even if they were not fully aware of the risks and benefits involved.

Hypothetical preference is different from actual choice. The present study assessed the value of hormonal chemoprevention perceived by subjects who are apparently at low risk of breast cancer. Preference would also be sensitive to the way in which information is presented (framing effects).[10, 11] For example, if a probability of being affected by breast cancer when the agent was not applied was given instead of a probability of being free of breast cancer when the agent was applied, respondents may have higher preference. Therefore, one should evaluate relative rather than absolute values for preference among the subjects. However, even considering such influences, it appears that reluctance to use this agent was not negligibly small in this population.

There was a large difference in preference score across the subjects. During the process of decision-making, tradeoffs between perceived benefits and risk of the agent would be involved. People make preference judgments based on the values (utility) they place on the possible outcomes. Utility theory postulates a simple mathemat-

68.2 and 2.3%, respectively, in college students and 3.6, 67.3 and 29.1%, respectively, in nursing school students. Multivariate analysis including school status and level of knowledge about hormones revealed that both factors were independently significantly associated with preference score at any efficacy level except for the 25% level. Refusal to take the agent at 100% level of breast cancer risk was still significantly associated with school status at all efficacy levels except 100%, but not with level of knowledge about hormones.

The distribution of HLC score among the subjects was as follows: 3 (3.1%), 20 (20.9%), 37 (38.5%), 28 (29.2%), and 8 (8.3%) for the 5 strata of HLC scores, 18–19, 20–24, 25–29, 30–34, and 35–38, respectively. Data were not obtained from two women. The means (SD) of HLC scores were 28.1 (4.5) in college students and 27.7 (4.6) in nursing school students. Age-adjusted HLC score was negatively correlated with preference score at any efficacy level of the agent, but the correlation was not statistically significant (Table V). Age-adjusted HLC score was significantly higher in those who rejected

ical model of decision-making in which people evaluate the expected utility (desirability) of alternative actions and select the action with the highest subjective expected utility (SEU).[12] The SEU of an action is the sum of the products of the probability of each possible outcome and its value. The observed great variation in preference judgments indicates that the expected utility of this agent greatly differs among subjects. Although subjects were not informed of possible unfavorable outcomes of this agent, subjective perception of risk of the agent must have influenced their determination of utility (preference) for this agent. I asked each subject to give her opinion about this therapy in an open-ended question. Among the respondents, 50% of college students and 75% of nursing school students mentioned a fear of possible adverse effects of this agent.

The data also indicate that the way subjects perceive probabilistic information about therapy is complicated. We can summarize possible outcomes of this therapy into two entities, i.e., benefits and disbenefits. The benefits are related to being free of breast cancer and disbenefits includes all undesirable states. According to the subjects, the appearance of adverse effects of the agent is important to them. Allotting the value 1 to the state of being completely free of breast cancer, the SEU for the agent in the jth scenario can be expressed as follows according to the SEU theory:

$$SEU_j = P_{1j} \times 1 + P_{2j}U_{2j}$$

where P_{1j} is the efficacy level of the agent and P_{2j} and U_{2j} are the subjective probability and utility of the undesirable state, or risk, in the jth scenario. If this agent has 100% efficacy and there is no possibility that the agent produces an undesirable state ($P_2 = 0$), perfect health status (utility = 1) is expected. The SEU_j corresponds to the preference score in the present study. As only the efficacy level of the agent was varied in the series of scenarios, we would expect that the perceived risk, $P_2U_{2j} = SEU_j - P_{1j}$, would be constant across the four scenarios. However, this was not the case (the mean values for $P_{2j}U_{2j}$ varied from -0.42 to -0.28, -0.13, and 0.02 for 100, 75, 50, and 25% efficacy levels, respectively), suggesting the simple SEU theory is not applicable.[13]

Nursing school students allotted lower utility score to this agent, indicating that they are more concerned about the potential risks of this agent. Respondents' knowledge about hormones also appeared to be linked with concern about the adverse effects of the agent. The level of knowledge about hormones was estimated subjectively. However, I also asked respondents what they knew about hormones in an open-ended question. Their answers were categorized into a total of 16 items, including names of individual female hormones, their functions, and so on. The Spearman correlation coefficients between the

number of items the subject gave and the reported level of knowledge about hormones was 0.50. The difference in preference between nursing school students and college students was not explained by the difference in levels of knowledge about hormones between the two groups. The difference in background knowledge about prevention agents and chemoprevention itself between the two groups may be related to the observed difference in preference for this agent. Although I could not obtain such information from individuals, I examined the curriculum at each school. The subjects in nursing school were first-year students who had learnt about preventive medicine in the introductory classes on medical science and the scientific background of nursing. However, chemoprevention was not dealt with in the textbooks for these classes. The subjects in college had completed a course on preventive medicine, but this did not include chemoprevention.

The data suggest that the concept of HLC can help to explain attitudes toward hormonal chemoprevention. Previous studies have indicated that more internally oriented individuals are more likely to engage in preventive health behavior.[14, 15] Students with an internal HLC orientation may tend to value more highly the preventive nature of the agent. It is also possible that those with an external HLC were less motivated to judge their preference for the agent and tried to avoid tradeoff.

It might have been difficult for the students to choose the point at which they would accept the agent. It should be noted that the measurements would have been impossible without use of personal interviews. I measured preference by using the standard gamble method, which is widely employed for measuring preferences for health status, but the response burden limits the use of this method in practice. Torrance[16] utilized a probability wheel, or chance board consisting of a disk with two movable, different-colored sections to help in the development of a rating scale for gambling. The chance of an outcome is proportional to the similarly colored area of the disk and respondents are asked to adjust the sections to represent the preference for the gamble alternatives. Use of such a visual aid might have been helpful. However, except for those who rejected the agent with any efficiency level at 100% level of breast cancer risk, no one gave the same risk level for different efficacy levels of the agent. They were apparently well able to think in terms of probabilities. Even after excluding those who refused the agent with any efficacy level at 100% level of breast cancer risk, the findings on preference related to school status, level of knowledge about hormones, and HLC score were essentially the same.

The reliability of the measurement of preference was checked by a test-retest method in another sample of 35 women aged between 20 and 46 years. The test-retest coefficients after two weeks were 0.84, 0.86, 0.82, and

0.73 for the agent with 100, 75, 50, and 25% of efficacy levels, respectively. The Spearman correlation coefficients between any two of the preference scores in the four settings were also high (ranging from 0.76 between the scores for the agent with 100 and 25% of efficacy levels to 0.91 between those with 75 and 50% of efficacy levels). As construct validity is rarely evaluated in the health preferences literature,[17, 18] I could not test the ability of the measurement to predict actual choice. Besides the scenarios for measuring preference for the breast cancer chemopreventive agent, I provided another similar set of hypothetical scenarios about preference for use of pills containing hormones to prevent obesity. In these scenarios, subjects were asked to determine the body weight at which they would start to take the agent with a given efficacy level. Respondents attitudes toward prevention of breast cancer and obesity must differ. Nevertheless, the correlation of the two cases ranged from −0.38 for 50% efficacy level to −0.48 for 25% efficacy level after controlling for body mass index. The relatively high negative correlation may indicate that the measure-

ments reflect the respondents' perceived risk of the agent containing hormones with reasonable validity.

The results presented here are considered preliminary and it may still be too early to measure preference for such an agent, as its risks and benefits are not established yet. However, an understanding of perceived risk of chemopreventive agents, especially those containing hormones, by measuring preference (=utility) is helpful to get an insight into the feasibility of future cancer chemoprevention. It also provides useful information on the value of promoting chemoprevention when beneficial effects are established. In the present study, for example, women who had a relatively high level of knowledge about hormones had a lower preference for the agent. There is a possibility that their perceptions of risk were influenced by undue emphasis on the adverse effects of hormone use, and that perceived risk exceeded actual risk. The relation between women's knowledge and behavior is complex and needs to be taken into account when planning a strategy for chemoprevention.

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