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Prevalence of hormone replacement therapy and user's characteristics: a community survey in Japan

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Abstract

Objectives: It is quite recently that much interest has been paid to the benefits of hormone replacement therapy (HRT) in Japan. We conducted a community survey in Japan in 1992 to examine the prevalence of HRT use and factors related to HRT use. *Methods:* A total of 8791 female residents aged 45–64 years old in a city of the Gifu Prefecture, Japan, responded to the questionnaire including medical and reproductive histories, lifetime occupational history, diet, exercise, smoking and drinking habits, and use of vitamin supplements or medications. The response rate was 94.2%. *Results:* Overall, 2.5% of women reported current use of HRT and 6.3% had used HRT previously. The highest prevalence of current use was found among postmenopausal women with surgical menopause (4.8%). Current users were more likely to have participated in cancer screenings, and to have used vitamin supplements or calcium during the past year. *Conclusions:* HRT use rate was 2.5% among female residents aged 45–64 years old in a Japanese community in 1992. Current users may have more regard for their health status.

Keywords: Hormone replacement therapy; Japan; Menopause; Prevalence

1. Introduction

Hormone replacement therapy (HRT) has been a successful and widespread treatment for women in the climacteric age for 30 years. Despite the popularity of HRT in the United States and European countries [1–7], it is only recently that attention has been paid in Japan to the benefits of HRT.

We notice that the effectiveness of HRT as a method of symptom management and protection against osteoporosis and cardiovascular diseases is introduced in current medical journals for Japanese physicians, although much of the information is based on data from American studies. Pharmaceutical companies have started active advertisements of medications used for HRT. Women's magazines have taken up the topic of the menopause and introduced HRT. However, little

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is known about the current prevalence of HRT use or the characteristics of the users. Several previous studies in other countries suggested that HRT users have more healthy lifestyles [8–10].

We surveyed the female residents in a community in Japan to determine the prevalence of current and past HRT users and explore the factors related to HRT use.

2. Methods

We analyzed the cross-sectional survey data from the Takayama Study. The study was initiated in 1992 to investigate the association between environmental and nutritional factors and cancers. All women aged between 35 and 101 living in a city of the Gifu Prefecture, Japan, were invited to the Takayama Study. The present study included women aged 45–64 years old. A total of 8791 women aged 45–64 responded to the health questionnaire distributed by volunteers in the city. The response rate was 94.2%.

The questionnaire requested information on medical and reproductive histories, lifetime occupational history, diet, exercise, smoking and drinking habits, and use of vitamin supplements or medications. Concerning HRT use, the first question asked the subjects whether they were currently taking or had taken sex hormones for menopausal symptoms. The two following questions were on age at start of HRT use and duration of use. Respondents who left the first question unanswered but filled out the remaining two questions were included in current/past users. Details on methods of data collection are described elsewhere [11].

Out of 8791 respondents aged 45–64 years old, 103 women left more than 40% of the questions unanswered and they were excluded from the analyses. The prevalence of HRT use was determined in 1992 among 8608 women aged 45–64 years old after excluding 80 women with a history of breast cancer because hormone use as treatment for this disease might not be distinguished from HRT in these women. Menopausal status at survey was determined by asking whether menstrual periods had stopped permanently or not and how old were they when this happened and for what reason (natural menopause, surgery, radiation, or medication). Women who indicated that their periods had been stopped by surgery, radiotherapy, or medication were classified as having surgical menopause.

The association between the categorized study variables and current HRT use was examined in logistic regression models. A multiple linear regression technique was utilized for testing the relationships of continuous variables to HRT use. These analyses were based on 215 current users and 7346 never-users. Although our data source was a cross-sectional survey, we favored factors known to appear prior to HRT. However, we are also interested in the user's attitudes toward the health even though they may be the effects of HRT. All the statistical analyses were performed by SAS software package [12].

3. Results

Overall, only 2.5% of the women aged 45–64 reported current use of HRT and 5.2% reported having used HRT (Table 1). Prevalence of current HRT use among postmenopausal women decreased with age. Postmenopausal women with surgical menopause were more likely to use or have used HRT than those with natural menopause in any age group.

More than half of the current as well as past users aged 45–64 years started HRT use between 45 and 54 years old (Table 2). As much as 40% ($n = 16$) of current users who had surgical menopause started HRT use before age 45 years, but 13.3% ($n = 17$) of those who had natural menopause did so (half of them had menopause before age 50 years).

Long-term (more than 5 years use) current or past HRT users were only 81 (0.9%) in this population (Table 2). Nineteen (23.5%) of them were surgically menopausal. About 25% of the current and 60% of the past users reported that the duration of HRT use was less than 1 year. Past users tended to be short-term users.

Current users were more likely to have participated in the screening for breast, uterus, stomach

and lung cancers and performed breast self-examination (Table 3). They were more likely to have used vitamin supplements during the past year. They also tended to have worked in retail shops or as saleswomen and to have had one or two births, but they were of borderline significance ($P = 0.07$, respectively). There was no significant association between current HRT use and education levels, use of oral contraceptive, smoking, age at menarche, age at first birth, or outcome of first birth. The means of height, weight, body mass index, and energy expenditures in physical activity were not different between current and never-users.

We performed multivariate analyses including age, menopausal status, and all the variables significantly related to current HRT use, i.e. attendance at cancer screenings, performing breast self-examination and weekly vitamin or calcium use (categories were listed in Table 3). As the variables for different kinds of vitamins uses were strongly correlated with each other, they were included in the model one by one. The results were not substantially changed except that the association of performing breast self-examination with HRT use became null.

Table 1
Prevalence of hormone replacement therapy use among 8608 female residents aged 45–64 years old in a Japanese community according to age and menopausal status

	Age (years)		
	45–54	55–64	Total
Total no.	4395	4213	8608[a]
Current users (%)	3.0	2.0	2.5
Past users (%)	6.2	6.5	6.3
Current/past users (%)[b]	9.4	9.0	9.3
Premenopause			
Total no.	2401	31	2432
Current users (%)	1.7	9.7	1.8
Past users (%)	4.9	9.7	5.0
Current/past users (%)	6.7	19.4	6.9
Postmenopause (natural)			
Total no.	1525	3505	5030
Current user (%)	3.9	2.0	2.5
Past users (%)	7.7	5.4	6.1
Current/past users (%)	11.9	7.8	9.0
Postmenopause (surgical)			
Total no.	375	453	828
Current users (%)	8.0	2.2	4.8
Past users (%)	9.1	15.9	12.8
Current/past users (%)	17.1	18.5	17.9

[a]Menopausal status was unknown for 318 women.
[b]Users with unknown status of current/past use are included.

4. Discussion

The prevalence of HRT use was markedly low in this Japanese community as compared with those in other countries. In the United States, a prevalence of 32% was derived from the community survey of postmenopausal women aged 50–65 years in California in 1986 [1]. The Massachusetts Women's Health Study reported that HRT use was 12.3% for women aged 45–55 years between 1981–1989 [2]. High prevalence rates were also reported in Finland (22% of women aged 45–64 years, 1989) [3], Sweden (7.5% of women at age 48 years) [4], the Netherlands (11.5% of women aged 45–60 years, 1990) [5], Australia (13.6% of women over the age of 40, 1991) [6], and France (8.1% of women aged 45–55 years, 1986) [7]. There were no studies in other countries which reported lower prevalence of HRT use than that observed in the present study.

We found only one previous report by Lock [13] on hormone use rate among Japanese women, although the study subjects were restricted to women aged 45–55 years. They were randomly sampled from female residents in Nagano, Kyoto, and Kobe, Japan, and the response rate was 76%. In this survey conducted in 1983–1984, out of 1225 women, 2.7% reported hormone use in the past 2 weeks. This use rate is similar to that observed in our study. We cannot compare these figures directly because the times when the studies were conducted and the study populations were different, but low prevalence of HRT use in Japan is marked.

As our study was based on a large sample of the general population and the response rate was high, the figures for prevalence were less likely to be affected by a non-response bias. The data were self-reported and we could not confirm the use or

Table 2
Age at start of hormone replacement therapy (HRT) and duration of HRT use for the 215 current and 543 past users according to age

	Current users			Past users		
	Age 45–54	Age 55–64	Total	Age 45–54	Age 55–64	Total
Age at start of HRT use						
−39	10 (7.7)	4 (4.7)	14 (6.5)	69 (25.5)	50 (18.4)	119 (21.9)
40–44	24 (18.5)	7 (8.2)	31 (14.4)	55 (20.3)	49 (18.0)	104 (19.2)
45–49	63 (48.5)	15 (17.7)	78 (36.3)	98 (36.2)	67 (24.6)	165 (30.4)
50–54	27 (20.8)	38 (44.7)	65 (30.2)	41 (15.1)	75 (27.6)	116 (21.4)
55+	0 (0.0)	16 (18.8)	16 (7.4)	0 (0.0)	20 (7.4)	20 (3.7)
NK[a]	6 (4.6)	5 (5.9)	11 (5.1)	8 (3.0)	11 (4.0)	19 (3.5)
Duration of HRT use						
−1	37 (28.5)	14 (16.5)	51 (23.7)	189 (69.7)	141 (51.8)	330 (60.8)
1–2	30 (23.1)	20 (23.5)	50 (23.3)	41 (15.1)	53 (19.5)	94 (17.3)
3–5	39 (30.0)	12 (14.1)	51 (23.7)	20 (7.4)	45 (16.5)	65 (12.0)
5–9	10 (7.7)	11 (12.9)	21 (9.8)	6 (2.2)	13 (4.8)	19 (3.5)
10+	6 (4.6)	22 (25.9)	28 (13.0)	5 (1.9)	8 (3.0)	13 (2.4)
NK	8 (6.2)	6 (7.1)	14 (6.5)	10 (3.7)	12 (4.4)	22 (4.1)

[a]NK, not known.

non-use of HRT. The probability that real users reported non-use is more likely to be greater than the probability that real non-users reported use. However, this misclassification might not have contributed to the substantial underestimate of the use rate in our study compared with the self-reported surveys conducted in other countries.

Although our cross-sectional data cannot assess the causal relationship, we can underline the potential importance of the factors related to HRT use. The previous study in Japan never examined these factors in relation to HRT use.

Most of the previous studies [2,7–10,14] found that surgical menopause was associated with HRT use, which was consistent with our result. Based on ages at menopause and when HRT use started, we assessed menopausal status prior to HRT use. Surgical menopause was significantly associated with subsequent HRT use (OR = 2.5) as compared with natural menopause.

Some studies reported that HRT users were thinner [1,2,10], exercised regularly [4,10,15], were more educated [1,9,16] and suggested that HRT users have a healthier profile. We found none of these associations. However, HRT users were more likely to have the cancer screening, which may indicate their concern about health. Relatively frequent use of vitamins or calcium among HRT users also suggests that HRT users have more regard for their health status. However, we have work-place and region based health insurance programs in Japan. Working women may be more likely to participate in cancer screening provided by the company. They may have more opportunities to be recommended HRT in the health service.

Although women with hysterectomy were more likely to have participated in cervical cancer screening, the association between participation in cervical cancer screening and HRT use was not affected greatly by adjustment for history of hysterectomy.

Some of the association found in our study might be affected by the relation between menopausal symptom and HRT use. For example, use of vitamin supplements may be regarded as one of the treatments for menopausal symptoms in some women.

The physicians' practice and belief may play a large role in the women's decision to take HRT. Doctors may be more ready to prescribe HRT for

Table 3
Age-adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for current use of hormone replacement therapy in relation to reproductive and lifestyle variables (based on 215 current and 7346 never-users)

Variables	Current user/never user (%)	OR	95% CI
Marital status			
Married	82.6/82.3	1.00	
Not married	17.4/17.7	1.02	(0.71–1.47)
Number of births			
1–2	71.3/64.9	1.00	
3+	24.4/27.5	0.81	(0.59–1.12)
Nulliparous	4.3/7.6	0.52	(0.51–1.03)
Years of education			
−8	14.0/17.7	1.00	
9–11	57.9/53.1	1.15	(0.74–1.78)
12+	28.0/29.2	0.97	(0.59–1.58)
Outcome of first birth			
Normal delivery	78.9/82.2	1.00	
Miscarriage/stillbirth/ extrauterine pregnancy	11.6/11.2	1.08	(0.69–1.68)
Artificial abortion	9.6/6.6	1.49	(0.92–2.43)
Age at first birth			
−25	61.1/64.4	1.00	
26+	38.9/35.6	1.74	(0.88–3.46)
Use of oral contraceptive			
Never	96.2/96.2	1.00	
Yes	3.9/3.8	0.94	(0.46–1.94)
Smoking			
Never	81.3/84.1	1.00	
Ever	18.7/15.9	1.20	(0.84–1.72)
Worked longest at retail shops or as saleswomen			
No	87.4/91.4	1.00	
Yes	12.6/8.6	1.52	(0.98–2.35)
Weekly use of vitamin supplements (prescribed) during past year			
Never	69.7/92.0	1.00	
Yes	30.3/8.0	5.51	(3.88–7.81)
Weekly use of vitamin supplements (non-prescibed) during past year			
Never	67.6/80.7	1.00	
Yes	32.4/19.3	2.04	(1.48–2.83)
Weekly use of calcium during past year			
Never	81.4/88.0	1.00	
Yes	18.6/12.0	1.77	(1.17–2.67)
Participance in cervical cancer screening			
Never	15.2/27.2	1.00	
Yes	84.8/72.8	2.04	(1.39–2.98)

Table 3 (continued)

Variables	Current user/never user (%)	OR	95% CI
Participance in breast cancer screening			
Never	77.0/83.5	1.00	
Yes	23.0/16.5	1.48	(1.06–2.06)
Participance in stomach cancer screening during past year			
Never	51.6/63.6	1.00	
Yes	48.4/36.5	1.66	(1.26–2.18)
Participance in lung cancer screening during past year			
Never	16.0/25.5	1.00	
Yes	84.0/74.5	1.82	(1.26–2.64)
Performance of breast self-examination			
Never	56.4/64.5	1.00	
Yes	43.6/35.6	1.36	(1.02–1.80)

women who had a hysterectomy because there was no concern about the risk of endometrial cancer for these women. However, it is unlikely that doctors would prescribe HRT selectively for women who had cancer screening.

The women who had frequent contact with the medical care system had more chances to receive recommendation for HRT use. The associations which were observed in our study may be confounded by the presence of certain diseases leading to frequent visits to health care. Our questionnaire included histories of 14 chronic or infectious diseases and 8 cancers. As we could not obtain the date at diagnoses of the diseases, we reserved discussion of the relationships between HRT use and these disease. We utilized the information on disease history as surrogate of women's contacts with the medical care system. Adjustments for histories of these diseases did not change our findings greatly.

According to the annual reports from pharmaceutical industry in Japan [17], production of 0.625 mg of conjugated estrogen, which is often used for HRT, increased 2-fold between 1992 (12.443 million tablets) and 1993 (25.594 million tablets). The figures for medroxyprogesteron, which is often used combined with conjugated estrogen for HRT, also showed an increase between 1992 (3.952 million tablets) and 1993 (5.340 million tablets) after showing a gradual decrease for several years. A major Japanese industry affiliated with Ayerst Laboratories in America reported that there had been an approximately 3-fold increase in Primarin production in the 3 years between 1991 and 1994 after a constant production level (personal communication). These data suggest that HRT use rate is rising in Japan and we need to repeat surveys to know the secular trend.

During the transition period, the use rate would vary by population. Some of the public medical hospitals in Japan have started clinics for women in the climacteric age and adopt HRT positively. Surveys of HRT use rates in different communities or populations are also required.

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