

The effect of physicians' advice and recommendations on compliance with hormone replacement therapy in the treatment of postmenopausal symptoms in Japanese women

— A prospective study —

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Abstract

A retrospective study was performed to determine compliance with hormone replacement therapy (HRT), and reasons for discontinuation. This study comprised 477 postmenopausal women who attended the women's psychosomatic and menopause clinic between January 1991 and December 2002. For the purposes of analysis, the postmenopausal women were classified into two groups. In group A (242 subjects), subjects were allowed to decide whether or not to suspend or discontinue the drug, taking their condition into account, after their symptoms were alleviated. In group B (235 subjects), individual women were informed as to the drug's excellent effects on osteoporosis and skin tissue before HRT was started and after their symptoms were alleviated. In group A, the percentage of women who were still on this therapy was 77.7%, 34.3%, 21.1%, and 8.7% at 3, 6, 12, and 24 months, respectively, after the start of therapy. Alternatively, in group B, the 24-month continuation rate was more than 50%. At 36 months (47.2%) and 60 months (38.7%), continuation rates were also significantly higher than those in group A ($P < 0.0001$). The leading reasons concerning the women's decision to discontinue HRT were improvement of symptoms (68.0% and 77.8% in groups A and B, respectively, $P = 0.408$). The incidence of the women's decision to discontinue HRT due to a fear of cancer was significantly higher in group A (10.8%) than in group B (2.8%) ($P = 0.008$).

In this study, the key factor affecting HRT compliance proved to be physicians' advice. This means that when HRT is administered to Japanese women with the objective of alleviating menopausal symptoms, high compliance rates can be expected provided individual patients are allowed to decide for themselves when HRT should begin and end.

Key words: climacteric medicine, compliance of hormone replacement therapy, physicians' advice

1. Introduction

The benefits of hormone replacement therapy (HRT) in relieving menopausal symptoms and the prevention of osteoporosis have been established (Tuppurainen et al., 1995). However, some reports, such as the Women's Health Initiative (WHI) randomized controlled primary prevention trial in 16,608 healthy postmenopausal health women (Women's Health

Initiative Investigators, 2002), demonstrated that HRT is not an appropriate prophylactic treatment for the prevention of coronary heart disease (Teede, 2002). A recent clinical survey of Japanese middle-aged women revealed that 31.8% of women thought the most appropriate target of HRT should be menopausal symptoms (Ushiroyama et al., 2003). Several studies have highlighted some of the reasons for hormone replacement discontinuation. Concerns

about safety and fear of cancer, especially, breast cancer, undesirable side effects, desire not to take hormones for long periods, and physicians' advice have been suggested (Chung et al., 1998; Oddens et al., 1997; Gass et al., 1997; Cano, 1995; Walsh et al., 1997).

To determine compliance with HRT (continuous administration of conjugated equine estrogen 0.625 mg with medroxyprogesterone acetate 2.5 mg a day) and reasons for discontinuation, a prospective study was performed in postmenopausal Japanese women with climacteric symptoms.

2. Patients and Methods

This study involved 477 postmenopausal women who attended the menopause clinic between January 1991 and December 2002. HRT for these women was started before the publication of the WHI report. Individual women were informed as to the advantages and risks involved in HRT, and only those who consented to the study were enrolled. Adequate information was also supplied on alternatives to HRT such as psychotropic drug therapy and herbal medicines. For the purposes of analysis, the postmenopausal women were classified into two groups. In group A (242 subjects), subjects were allowed to decide whether or not to suspend or discontinue the drug, taking their condition into account, after their symptoms were alleviated. In group B (235 subjects, individual women were informed as to the drug's favorable effects on osteoporosis and skin tissue, risks for uterine endometrial cancer, breast cancer, and venous thrombosis before HRT was started and after their symptoms were alleviated. Each woman had her bone density measured and was given fracture prevention advice every 6 months.

Statistical analyses were performed with the Statview ver. 5.0 software program (Abacus

Concepts, Berkeley, CA, USA). All values are expressed as the mean±SD. We used the Mann-Whitney two independent sample test to evaluate potential differences between groups each time. A significance level of $P < 0.05$ was chosen.

3. Results

Table 1 shows the means of the variables analyzed in this study in patients from the two groups. No difference was found between the groups regarding any of the variables.

1) The effect of physicians' advice on compliance with HRT

In group A, the percentage of women who were still on this therapy was 77.7%, 34.3%, 21.1%, and 8.7% at 3, 6, 12, and 24 months, respectively, after the start of therapy (Fig. 1). Thus, more than half of all patients discontinued HRT within 6 months. In 159 subjects, who had discontinued HRT after less than 6 months of administration, 77.4% (123/159) of them experienced symptom improvement. Only 18.2% (29/159) dropped out because of fear of cancer, undesirable side effects, and friends' misleading information about HRT. The two and five-year continuation rates were only 8.7% and 4.5%, respectively. Alternatively, in group B, the 24-month continuation rate was more than 50%. At 36 months (47.2%) and 60 months (38.7%), continuation rates were also significantly higher than those in group A ($P < 0.0001$).

2) The reasons for discontinuation of HRT

Table 2 shows the common reasons for the women's decision to discontinue HRT. The leading reason was the improvement of symptoms (68.0% and 77.8% in groups A and B, respectively, $P=0.408$). The incidence of the women's decision to discontinue HRT due to a

Table 1 Mean initial values of the variables in patients with HRT use

Variables	Groups		P-value
	No physician's advice	Appropriate physician's advice	
No.	242	235	
Age (year)	54.37±8.29	54.22±8.44	0.845
Age at menopause (year)	50.5 ±4.33	50.3 ±4.35	0.615
Duration of menopause (year)	4.28±0.77	4.23±0.79	0.484
BMI (Kg/m ²)	23.1 ±3.0	22.9 ±3.2	0.482
Smoker (%)	15.7	15.3	0.921
Hyperlipidemia (%)	37.2	36.6	0.998
Osteopenia & Osteoporosis (%)	38	38.3	0.967

BMI: body mass index

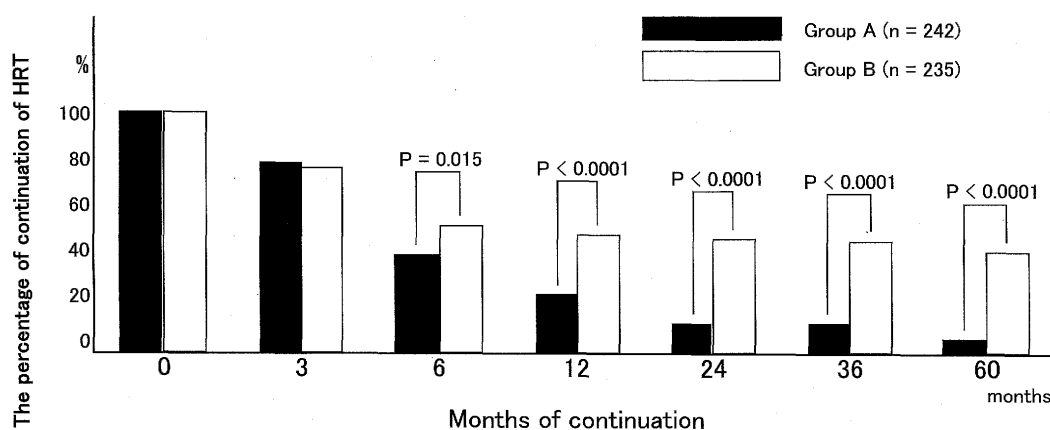


Fig. 1 Compliance with HRT in the treatment of menopausal symptoms (group A: n=242, group B: n=235). In 159 subjects, who had discontinued at 6 months administration, 123 (77.4%) showed improvement of symptoms and 29 (18.2%) had dropped out

Table 2 Reasons for discontinuation of HRT in two groups

Reasons	Groups			P-value
	No physician's advice	Appropriate physician's advice		
Improvement of symptoms	157 (68.0%)	112 (77.8%)		0.408
Side effects	11 (4.8%)	7 (4.9%)		0.968
Irregular genital bleeding	13 (5.6%)	5 (3.5%)		0.364
Breast symptoms	8 (3.5%)	3 (2.1%)		0.454
Fear of cancer	25 (10.8%)	4 (2.8%)		0.008
Fear of thrombosis	7 (3.0%)	7 (6.1%)		0.382
Loss of follow-up	7 (3.0%)	5 (4.4%)		0.819
Others	3 (1.3%)	1 (0.9%)		0.583
Total	231 (100%)	144 (100%)		

fear of cancer was significantly higher in group A (10.8%) than in group B (2.8%) ($P=0.008$). Although no significant difference was observed, the incidence of discontinuing due to a fear of thrombosis was 3.0% and 6.1% in groups A and B, respectively ($P=0.382$).

4. Discussion

Groeneveld et al. (1998) demonstrated that only 8% of women remained on HRT for more than 2 years, indicating that the initiation of HRT in general practice was to alleviate menopausal symptoms such as hot flashes rather than to prevent long-term postmenopausal conditions linked to estrogen deficiency. Our results on HRT compliance at 24 months (8.7%) are comparable to those found in Groeneveld's report (Groeneveld et al., 1998). It has been reported that an explanation given to postmenopausal women of the potential beneficial effects on health and an active recommendation of HRT improved compliance to 71.1% at 5 years (Leung et al., 2001).

In this study, physicians' advice significantly increased compliance after 6 months of taking HRT. From a clinical viewpoint, it is important to recognize that HRT is not just indicated in the treatment of menopausal symptoms, which is how it has been used for a long time, but increasing attention is being paid to the prevention of postmenopausal diseases linked to estrogen deficiency, such as osteoporosis. In this study, the key factor affecting HRT compliance proved to be physicians' advice. It was also found that if the awareness and intention of individual women (who think that the goal of treatment is to alleviate symptoms) are fully respected and the physician refrains from giving advice on continuation of the drug, 70% of patients discontinue HRT in less than one year (following alleviation or disappearance of symptoms) and less than 10% of patients continue receiving the therapy for one year or longer. This means that when HRT is administered to Japanese women with the objective of alleviating menopausal symptoms, high compliance rates can be expected

provided individual patients are allowed to decide for themselves when HRT should begin and end. In this situation, only a very small percentage of these patients will continue therapy for 5 years or more.

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