

Duration of hormonal replacement therapy in general practice; a follow-up study

F.P.M.J. Groeneveld^{a,*}, F.P. Bareman^a, R. Barentsen^d, H.J. Dokter^a,
A.C. Drogendijk^b, A.W. Hoes^{a,c}

^a Department of General Practice, Erasmus University Rotterdam, Postbox 1738, 3000 DR Rotterdam, The Netherlands

^b Department of Obstetrics & Gynaecology, Erasmus University Rotterdam, Rotterdam, The Netherlands

^c Department of Epidemiology & Biostatistics, Erasmus University Rotterdam, Rotterdam, The Netherlands

^d Department of Obstetrics & Gynaecology, University Hospital Vrije Universiteit, Amsterdam, The Netherlands

Received 30 September 1996; received in revised form 21 January 1998; accepted 30 January 1998

Abstract

Objectives: To assess the mean duration of use of HRT in general practice and to identify determinants of the duration of HRT use. *Methods:* A general population of 1689 women aged 45–60 years and enlisted in five group practices of general practitioners were followed for 9 months to trace first HRT prescriptions. All 103 women who were prescribed HRT were followed for a period of 2.25 years. Duration of HRT was assessed by using the data provided on the dispensing of HRT. Possible determinants of duration of use, such as attitude towards menopause, menopausal status and another six variables were measured by means of a questionnaire. *Results:* None of the 103 women received HRT for a preventive purpose; the main indication was menopausal complaints. More than 60% of the women stopped their HRT within 6 months and only 8% of the women remained on HRT for more than 2 years. The mean duration of use was 7 months. Determinants that significantly predicted the duration of HRT use were age, attitude towards treatment of the menopause and the group practice. *Conclusions:* The mean duration of HRT use is very short, despite the fact that the most prevalent indication is the alleviation of menopausal symptoms. Apparently, Dutch women are presently unwilling to take HRT for longer periods. © 1998 Elsevier Science Ireland Ltd. All rights reserved.

Keywords: Hormonal replacement therapy; General practice; Menopause; Dutch women

1. Introduction

In the USA the prescription of estrogens in menopausal women more than doubled in the

* Corresponding author.

period 1960 to 1974. The positive attitude towards postmenopausal estrogen use in this period is reflected by publications like Wilson's widely read book 'Feminine Forever' in which estrogens were strongly recommended [1]. In Sweden the consumption even trebled between 1973 and 1977 [2]. A drop in the use of estrogens appeared in the late 1970s. This was probably due to the commotion about reports of a strong association between estrogen replacement therapy and endometrial cancer [3,4]. Consensus exists that, in addition to estrogens, women with an intact uterus should be given progestogens in order to prevent endometrial cancer [5]. As a consequence of the acclaimed beneficial effects of hormone replacement therapy (HRT) on osteoporosis and cardiovascular disease, a renewed interest in HRT has emerged [6,7]. In recent years, however, conflicting data became available concerning the risk of breast cancer associated with these drugs [8].

Appropriate duration of HRT is about 1–2 years for the main indications for HRT, i.e. the alleviation of vasomotor symptoms, and at least 3–5 years to prevent osteoporosis and cardiovascular diseases [9–12]. The few studies that assessed the duration of use of HRT after its initiation, indicate that estrogens are stopped earlier than the indication would require [13–15]. This has been attributed to the fear of cancer, discomfort associated with the inherent withdrawal bleedings or side effects such as breast tenderness [16–19].

The aims of our study were (i) to assess the duration of use of HRT in general practice and (ii) to determine which variables predict the duration of HRT use.

2. Methods

2.1. Recruitment

This study is part of a larger study aimed at assessing the relationships between climacteric, well-being, women's attitude towards menopause and medical attention [20]. In short, from the municipal authorities of Krimpen aan den IJssel, a commuter suburb of Rotterdam with approxi-

mately 28000 inhabitants, names and addresses of all 2729 women aged 45–60 years were obtained. These women were all enlisted in one of the five group practices of general practitioners in Krimpen aan den IJssel. In May 1990 they were sent a questionnaire; 1947 women responded (response, 71.3%). A random sample ($n = 55$) was taken of the non-respondents in order to evaluate how representative the respondent group was. They were approached by telephone and 52 participated (response 95%). The comparison between respondents and non-respondents revealed no statistically significant differences in age, menopausal status, hysterectomy, estrogen therapy, level of education, work outside the home or medical attention.

To measure the incidence of first HRT prescriptions (i.e. prescription for women who did not use estrogen therapy within 6 months preceding the questionnaire), dispensing data were provided by the two pharmacies in Krimpen aan den IJssel. Both pharmacies are computerised. The measurement period lasted from 1 July 1990 until 1 April 1991. Of the 1947 women who returned the questionnaire, 220 women who had used estrogen therapy in the 6 months preceding 1 July, and the seven women who used progestogens without estrogens, were excluded. Further, 31 women could not be traced in the pharmacies' database. The remaining 1689 women were included in the study and followed for a period of 9 months to monitor first HRT prescriptions. In total, 103 women (incidence in 9 months, 6.2%) were prescribed HRT. This cohort forms the basis of the present study. These 103 women were followed, from the initiation of HRT, for a period of 2.25 years.

The study received approval from the Medical Ethical Committee of Erasmus University and Academic Hospital Dijkzigt in Rotterdam.

2.2. Measurements

The duration of HRT use of the 103 women in the cohort was assessed by using dispensing data provided by the two local pharmacies. For each HRT dispensing the expected final date of use was computed. If the interval between the computed final date and the date of the next dispensing of

Table 1

Mean duration in months of the continuous use of hormonal replacement therapy according to type of application in general practice

	<6 months	6–12 months	12–18 months	18–24 months	>24 months
All women (<i>n</i> = 103) (%)	64	21	4	3	8
Transcutaneous (<i>n</i> = 16) (%)	69	31	0	0	0
Oral (<i>n</i> = 49) (%)	61	20	4	2	12
Creams (<i>n</i> = 24) (%)	79	21	0	0	0
Tibolone (<i>n</i> = 14) (%)	93	7	0	0	0

HRT was less than 42 days, the use of HRT was considered to be continuous, irrespective of a possible change of estrogen application. If the next dispensing occurred more than 42 days after the computed final date of the previous dispensing, the HRT prescription was considered to be interrupted. The period of 42 days was chosen to make sure that short-term beneficial effects would have disappeared. If a next dispense occurred before the computed final date of the previous dispense, the overlapping time was counted only once in the computation of the total period of HRT prescriptions. Several variables that could influence the duration of HRT use were measured. The indication for HRT was assessed retrospectively by asking the women's general practitioners about their reason for prescription, with the assistance of the patient's records.

Three attitude clusters towards menopause were distinguished: two clusters encompass items reflecting the idea that 'menopause is advantageous' and 'menopause is disadvantageous', and one cluster encompasses items reflecting the idea that 'menopause should be treated (medically)'. The women were asked to rate their opinion on all items on a scale from 1 (totally agree) to 5 (totally disagree). Per cluster mean scores were computed.

To ascertain menopausal status according to last menstrual bleeding, women were classified into pre-, peri- and postmenopausal on the basis of the menstrual history. Premenopausal women had had a regular menstruation pattern in the preceding 12 months. Women were classified as perimenopausal if irregular cycles or amenorrhea had developed in the 12 months prior to the questionnaire. Women were categorised as post-

menopausal if the last menstrual bleeding occurred at least 12 months previously. Women who had undergone hysterectomy were categorised as a separate group.

The methods used to measure the other variables, such as type of application, education, hysterectomy, use of contraceptive pill, smoking and group practice are shown in Tables 1 and 2.

2.3. Data analysis

The attitude measurements were dichotomised around the median. For each category of a possible determinant, the mean duration (in months) of the prescription of HRT within a period of 2.25 years was computed. Whether the submeans differed significantly from each other was tested by means of analysis of variance. All variables for which these differences were significant at a $P < 0.10$ level were entered into a multiple regression analysis, with the duration of HRT use as the dependent variable.

3. Results

The indications for the prescription of HRT were relatively short term, i.e. to relieve vasomotor symptoms or menstruation disturbances. The mean duration of use of hormone replacement therapy of the 103 women was 7 months (standard deviation, 7.1; range, 0.5–27 months). Table 1 and Fig. 1 show the duration of use for all women and for the women on different applications of HRT. Within 6 months, more than 60% of the women stopped using HRT. After 2 years, 8% of the women were still using HRT. Tibolone,

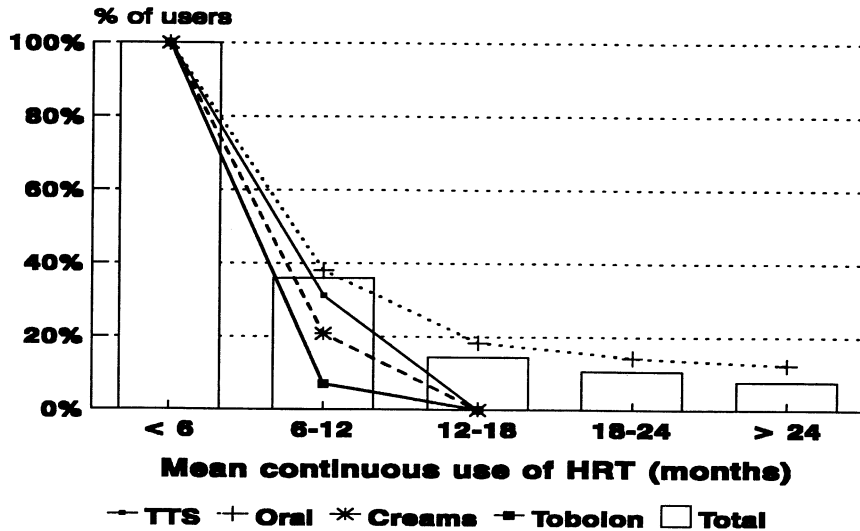


Fig. 1. The mean duration in months of the continuous use of HRT, according to the type of application ($n = 103$ women).

which does not provoke withdrawal bleedings, showed the highest withdrawal rate within 6 months (93%), whereas these figures were 79, 69 and 61% for creams, transcutaneous and oral applications (excluding tibolone), respectively.

Table 2 shows the association between several other variables and the mean duration of HRT use (in months). Three of these variables appear to be significantly related to the duration of HRT use. Women having a more positive attitude towards treatment before the onset of HRT, used HRT on average 3.4 months longer than women with a more negative attitude. Older women stayed on HRT shorter than younger women. The mean duration of HRT use for women aged 45–50, 50–55 and 55–60 years were 8.9, 6.0 and 4.4 months, respectively. The mean duration of HRT appeared to vary, according to the group practice, from 4.4 (group practice A) to 10.4 months (group practice D). Postmenopausal women used HRT for a somewhat shorter period than pre- and perimenopausal women.

The multivariate regression analysis showed that the group practice and the attitude cluster 'The menopause should be treated', but not age, were independent predictors of the duration of HRT use. Compared to practice group A, the women in the other group practices B, C, D and

E used HRT 3.7, 3.0, 3.2 and 3.3 months longer, respectively (these numbers represent regression weights). For the attitude cluster, the 50% of women having a more positive attitude towards treatment of the menopause were used as the reference category. Compared to these women, the 50% of women having a more negative attitude used HRT on average 3.1 months less.

4. Discussion

In this follow-up study of 103 women, who started to use hormonal replacement therapy (HRT) in general practice, more than 60% stopped their HRT within 6 months, and only 8% of the women remained on HRT for more than 2 years. The mean duration of use was 7 months. The main determinants of the duration of HRT use were type of application of HRT, age group, attitude towards treatment of the menopause before onset of HRT, and the women's group practice.

Few studies assessed the duration of use of HRT. Wren and Brown found that, of 100 women, 61% continued therapy beyond 1 year [14]. Barlow et al. found that, after 2 years, only 15% of the women were still on HRT [21]. We

Table 2
Mean duration in months of use of HRT according to different characteristics

Determinant	Mean	Standard deviation	<i>P</i> value
Attitudes			
Menopause is disadvantageous			0.14
Below median ^a	6.3	6.1	
Above median ^b	8.9	9.3	
Menopause is advantageous			0.76
Below median ^a	7.7	8.5	
Above median ^b	7.2	7.0	
Menopause should be treated			0.03
Below median ^a	8.7	8.4	
Above median ^b	5.3	5.9	
Sociodemographic variables			
Age group (years)			0.03
45–50	8.9	8.6	
51–55	6.0	6.0	
56–60	4.4	3.4	
Education			0.78
Low	6.6	7.4	
Middle	6.7	7.0	
High	8.1	7.9	
Gynaecological variables			
Menopausal status according to last menstrual bleeding			0.10
Premenopausal	9.1	8.6	
Perimenopausal	8.4	7.9	
Postmenopausal	5.0	4.9	
Hysterectomy			0.36
No	7.3	7.3	
Yes	5.8	6.3	
Contraceptive pill			0.37
Never used	5.6	5.8	
Formerly used	7.2	7.3	
Other variables			
Smoking			0.61
Never/ever	6.3	6.3	
1–15 per day	8.4	9.3	
>15 per day	7.4	8.1	
Group practice			0.05
A	4.5	4.0	
B	9.3	8.3	
C	5.8	6.1	
D	10.4	10.0	
E	5.0	3.3	

^a Below median: 50% of the women who agree most with the items.

^b Above median: 50% of the women who disagree most with the items.

found the same pattern, although the percentage of women who stopped HRT is higher in our study.

The majority of women in our study stopped using HRT within 6 months. This indicates that women take HRT for short-term effects, notably

to alleviate symptoms such as flushes. This was confirmed by the women's general practitioners. Roberts reported that 80% of women use HRT primarily to relieve menopausal symptoms, while only 6% use it as a prophylactic against osteoporosis [22].

If prevention of cardiovascular diseases and osteoporotic fractures were to become more important indications, a longer use of HRT seems likely.

Draper and Roland [23] suggested another important reason for early withdrawal from HRT: they found that 50% of women judged the risks of HRT higher than the benefits. Especially, the fear of cancer may be crucial.

Tibolone, which does not provoke withdrawal bleedings, showed the highest withdrawal rate within 6 months (93%). It is somewhat surprising that treatment which does not give withdrawal bleeding is used for a shorter duration than regimens that induce bleeding, since the study of Dören et al. on continuous combined HRT indicates the opposite [24]. Therefore, we doubt whether bleeding is the relevant factor.

Our study suggests that the role of the general practitioner influences the duration of HRT use. This is in accordance with the study of Ferguson et al., who also found that the physician influences the duration of HRT use [25]. Doctors probably vary in their opinion about the necessity of chronic use of HRT, and thus influence their patient's behaviour [26,27].

The attitude towards treatment of the menopause was a strong predictor of the duration of HRT use. In an earlier study we established that this attitude was also a predictor of the initiation of HRT [28]. Sinclair et al. also reported that a positive attitude towards treatment was related to a longer duration of HRT use [29].

In a univariate analysis younger women seemed to comply more with HRT use than older women. Harris et al. also reported that menopausal women who used estrogens were relatively young [30]. Probably older women stop sooner when they start a particular treatment (in the case of alleviation of complaints) at a later age, when complaints can be supposed to have disappeared sooner as well. However, when multivariate analysis is used, the effect of age is no longer statistically significant, whereas the effects of group practice and a positive attitude about treatment of the menopause remain.

A disadvantage of our study is that we did not measure the reasons for stopping HRT. Another

limitation lies in the fact that we evaluated the indication retrospectively, using both the patients' records and information from the general practitioners. Further, the relatively small sample size and the heterogeneity of HRT use (creams, tablets, transdermal) limits the possibility to study a wide variety of potential determinants of duration of HRT use, such as hysterectomy or menopausal status.

An advantage of our pragmatic study concerns the opportunity to observe duration and determinants of use as it occurs in daily medical practice.

We conclude that the mean duration of HRT use is short, despite the fact that the main indication was alleviation of menopausal symptoms. Apparently, Dutch women are presently unwilling to take HRT for longer periods.

Acknowledgements

This work was supported by grants from Ciba-Geigy, Schering and Wyeth-Ayerst. We would like to thank Mrs De Haan-Meyneel for her helpful comments and the pharmacists P.K. Schot and B.A.J. Geurts for helping with the follow-up of HRT use.

References

- [1] Wilson RA. *Feminine Forever*. New York: Evans, 1966.
- [2] Pedersen SH, Jeune B. Prevalence of hormone replacement therapy in a sample of middle-aged women. *Maturitas* 1988;9:339–45.
- [3] Smith DC, Prentice R, Thompson DC, Herman WL. Association of exogenous estrogen and endometrial carcinoma. *New Engl J Med* 1975;293:1164–7.
- [4] Antunes CMF, Stolley PD, Rosenheim NB. Endometrial cancer and estrogen use. Report of a large case-control study. *New Engl J Med* 1979;300:9–13.
- [5] Whitehead M, Lobo RA. The consensus conference: progestagen use in postmenopausal women. *Lancet* 1988;ii:1243–4.
- [6] Riggs BL, Melton LJ III. The prevention and treatment of osteoporosis. *New Engl J Med* 1992;327:620–7.
- [7] Stampfer MJ, Colditz GA. Postmenopausal estrogens and coronary heart disease: a review of epidemiologic evidence and a metaanalysis. *Prev Med* 1991;20:47–63.
- [8] Colditz GA, Egan KM, Stampfer MJ. Hormonal replacement therapy and risk of breast cancer: results from

- epidemiologic studies. *Am J Obst Gynecol* 1993;168:1473–80.
- [9] McKinlay S, Jefferys M. The menopausal syndrome. *J Prev Soc Med* 1974;28:108–15.
- [10] Riggs BL, Melton LJ III. The prevention and treatment of osteoporosis. *New Engl J Med* 1992;327:620–7.
- [11] Consensus Development Conference. Diagnosis, prophylaxis, and treatment of osteoporosis. *Am J Med* 1993;94:646–50.
- [12] Stampfer MJ, Colditz GA, Willet WC, et al. Postmenopausal estrogen therapy and cardiovascular disease. Ten-year follow-up from the Nurses' Health Study. *New Engl J Med* 1991;325:756–62.
- [13] Ryan PJ, Harrison R, Blake GM, Fogelman I. Compliance with hormone replacement therapy (HRT) after screening for postmenopausal osteoporosis. *Br J Obstet Gynaecol* 1992;99:325–8.
- [14] Wren BG, Brown L. Compliance with hormonal replacement therapy. *Maturitas* 1991;13:17–21.
- [15] Speroff T, Dawson NV, Speroff L, Haber RJ. A risk-benefit analysis of elective bilateral oophorectomy: effect of changes in compliance with estrogen therapy on outcome. *Am J Obstet Gynecol* 1991;164:165–74.
- [16] Hahn RG. Compliance considerations with estrogen replacement therapy: withdrawal bleeding and other factors. *Am J Obstet Gynecol* 1989;161:1854–8.
- [17] Doren M, Reuthers G, Minne HW, Schneider HP. Superior compliance and efficacy of continuous combined oral estrogen-progestogen replacement therapy in postmenopausal women. *Am J Obstet Gynecol* 1995;173:1446–51.
- [18] Draper J, Roland M. Perimenopausal women's view on taking hormone replacement therapy to prevent osteoporosis. *Br Med J* 1990;300:786–8.
- [19] Barentsen R, Groeneveld FPMJ, Bareman FP, Hoes AW, Dokter HJ, Drogendijk AC. Women's opinion on withdrawal bleeding with hormone replacement therapy. *Eur J Obstet Gynecol Reprod Biol* 1993;51:203–7.
- [20] Groeneveld FPMJ, Bareman FP, Barentsen R, Dokter HJ, Drogendijk AC, Hoes AW. Relationships between attitude towards menopause, well-being and medical attention among women aged 45–60 years. *Maturitas* 1993;17:77–88.
- [21] Barlow DH, Grosset KA, Hart H, Hart DM. A study of the experience of Glasgow women in the climacteric years. *Br J Obstet Gynaecol* 1989;96:1192–7.
- [22] Roberts PJ. The menopause and hormone replacement therapy: views of women in general practice receiving hormone replacement therapy. *Br J Gen Pract* 1991;41:421–5.
- [23] Draper J, Roland M. Perimenopausal women's views on taking hormone replacement therapy to prevent osteoporosis. *Br Med J* 1990;300:786–8.
- [24] Doren M, Reuthers G, Minne HW, Schneider HP. Superior compliance and efficacy of continuous combined oral estrogen-progestogen replacement therapy in postmenopausal women. *Am J Obstet Gynecol* 1995;173(5):1446–51.
- [25] Ferguson KJ, Hoegh C, Johnson S. Estrogen replacement therapy: a survey of women's knowledge and attitudes. *Arch Intern Med* 1989;149:133–6.
- [26] Bryce FC, Lilford RJ. General practitioners use of hormone replacement therapy in Yorkshire. *Eur J Obstet Gynecol Reprod Biol* 1990;37:55–61.
- [27] Backe B, Hunskaar S, Skolbekken JA. General practitioners attitude to oestrogen prescription in the menopause: a national survey in Norway. *Scand J Prim Health Care* 1992;10:179–84.
- [28] Groeneveld FPMJ, Bareman FP, Barentsen R, Dokter HJ, Drogendijk AC, Hoes AW. Determinants of first prescription of hormone replacement therapy: a follow-up study among 1689 women aged 45–60 years. *Maturitas* 1995;20:81–9.
- [29] Sinclair HK, Bond CM, Taylor RJ. Hormone replacement therapy: a study of women's knowledge and attitudes. *Br J Gen Pract* 1993;43:365–70.
- [30] Harris RB, Laws A, Reddy VM, King A, Haskell WL. Are women using postmenopausal estrogens? A community survey. *Am J Public Health* 1990;80:1266–8.