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Hormonal substitution during menopause: what are we treating?

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Abstract

Objectives: It is suggested that during menopausal transition, women with vasomotor symptoms benefit from HRT, (hormone replacement therapy) whereas, the use of HRT for other cognitive–vegetative symptoms is questionable. *Methods*: The occurence of menopausal complaints and depressive symptoms was assessed cross-sectionally in 5896 Dutch Caucasian women (47–54 years) of a large community sample in the city of Eindhoven, The Netherlands. Menopausal complaints were assessed using a 22 items self-rating scale (consisting of a vasomotor , uro-genital and a cognitive–vegetative subscale). Depressive symptoms were assessed using the Edinburgh depression scale (EDS). Differences in mean scores were analysed between groups using ANOVA. The independent relationship of depressive symptoms to the intensity of menopausal complaints was assessed, by multiple linear regression analysis. *Results*: Women using HRT showed the highest scores on all subscales. Oral contraceptive users had significantly lower scores on the vasomotor subscale compared to HRT users and to non users. Depressive symptoms contributed the most, to the explained variance on scores on the menopausal subscales. *Conclusions*: Women during menopause presenting several complaints, other than vasomotor origin might be suffering from underlying depression which makes it questionable to prescribe HRT for the latter symptoms.

Keywords: Menopausal transition; Linear regression analysis; Vasomotor

1. Introduction

According to a recent WHO report [1] depression has become a major health problem. The prevalence rate is high, the burden of illness extensive and, as a consequence, the economic costs are considerable [2]. A recent survey in the Netherlands revealed a point prevalence of 8% in the general population [3]. Despite the fact, that treatment strategies have markedly improved, it is estimated that only 20% of depressed patients receive adequate therapy [1]. It is thought that the non awareness of signs and symptoms of depression in the general population, could partly explain the underestimation of depression as a major health problem. Moreover, in up to 50% of

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depressed patients who visit their general practitioner, the symptoms are misdiagnosed [4] and therefore accurate detection should result in more appropriate therapy.

In general practice, it is well known that patients presenting various and often vague complaints, may be suffering from underlying depression. Also, during menopausal transition, it is said that 50–70% of women experience all kinds of somatic and emotional symptoms [5]. While vasomotor (flushing) and uro-genital (vaginal dryness) symptoms are widely recognised as being a direct consequence of the declining estrogen production during menopausal transition, there is much debate concerning the specificity of cognitive, vegetative and emotional symptoms in the climacteric. Nevertheless, for the latter symptoms as well, a huge amount of estrogens are prescribed (hormone replacement therapy, HRT) to relieve the inconvenience in these women. It is a matter of speculation whether women, who present a whole range of vague complaints are in fact suffering from underlying depression. If so, it could be questioned whether the prescription of hormone replacement therapy for these symptoms is justified.

In a large community sample of women, ranging in age from 47 to 54 years, we investigated the extent to which perimenopausal complaints are associated with depression.

2. Material and methods

2.1. Subjects

Between September 1994 and 1995 all women ($n = 8503$) born between 1941 and 1947 in the city of Eindhoven, The Netherlands, were invited to participate in a screening programme for osteoporosis: the Eindhoven perimenopausal osteoporosis study (EPOS) [6]. A total of 6648 women (78%) consented to participate. During the screening, an accurate medical history was obtained. Subsequently, the women were asked to complete several questionnaires at home and to return these within 1 week after screening.

Because of possible language problems, only Dutch Caucasian women (5896, 89%) were included in the analysis. Ninety-two percent (5424) returned the questionnaires, 76% of which (4146) were correctly completed. In order to avoid any possible bias from gynaecological operations, all women who had undergone a hysterectomy and/or a uni- or bilateral ovariectomy ($n = 1117$) were excluded from the analysis. Therefore, the data analysis covers the remaining 3029 women (Table 1). No differences in the characteristics were found between the original sample and the sample from this study (mean age, educational level, employment, marital status, having had children, mean BMI and menopausal status.). Estrogen use, was somewhat higher in the original sample (14 vs 10%), which was largely explained by the presence of ovariectomised women. Of the 3029 women, 377 (12%) still used hormonal oral contraception (OC), 320 (10%) were on HRT, while 2332 women were not using any estrogen therapy.

The study was approved by the medical ethics committee of the St Joseph's Hospital in Veldhoven, The Netherlands.

2.2. Assessment of menopausal complaints

The occurrence of menopausal complaints was assessed using the 24-item self-rating scale which has been validated earlier [7]. Moreover, we added three items: vaginal dryness, pain during intercourse and waking up at night, which, according to the literature, are also specific for the transition to menopause [8,9]. The psychometric properties of this 27-item self-rating scale were analysed in the women not using any hormonal substitution ($n = 2332$). Principal compound factor analysis showed that 22 items loaded significantly and covered three subscales: a vasomotor subscale (three items: flushing, day sweating, night sweating, range 0–9), an uro-genital subscale (four items: vaginal dryness, pain with cohabitation, vaginal itching and burning on micturation, range 0–12) and a cognitive–vegetative subscale (15 items: irritability, lack of energy, depressed mood, lack of self confidence, agitation, forgetfulness, tiredness on waking, headache, tiredness, dizziness, muscle pain, shortness of breath, restless

legs, palpitations and insomnia, range 0–45) with a Cronbach's alpha of 0.90, 0.88, and 0.65, respectively, reflecting adequate internal consistency.

2.3. Assessment of depressive symptoms

Depressive symptoms were assessed using the Edinburgh depression scale (EDS), which is a ten-item self-rating scale originally designed for use in postpartum women and recently validated in middle aged non childbearing women [10,11,15]. Scores varied between 0 and 30 (with higher scores indicating more depressive symptomatology) with a commonly used cut-off score of 12.

2.4. Statistical analysis

Statistical analysis was performed using the statistical products and service solutions (SPSS). Correlations between the various scales were analysed by means of Pearson's correlation coefficient (using two-tailed P-values). Differences in mean scores on several scales were analysed between groups, using ANOVA. In order to detect differences between these groups, a post hoc anal-

Table 1
Characteristics of the samples of Dutch Caucasian women in the EPOS study

	Total sample		Study sample	
	$n = 5896$	(%)	$n = 3029$	(%)
Mean age (year) (SD)	50.0	(2.1)	49.8	(2.1)
Educational level				
Primary school	668	(12.8)	324	(10.7)
Lower professional education	1821	(35.0)	1009	(33.3)
Secondary modern education	1379	(26.5)	830	(27.4)
Secondary professional education	306	(5.9)	188	(6.2)
High modern education	380	(7.3)	245	(8.1)
High professional education	562	(10.8)	382	(12.6)
Academic	83	(1.6)	51	(1.7)
Employment	1892	(32.1)	1087	(35.9)
Marital status				
With partner	4492	(76.2)	2393	(79.0)
Single	1404	(23.8)	636	(21.0)
Children				
No	772	(13.1)	424	(14.0)
1	907	(15.4)	454	(14.9)
≥ 2	4217	(71.5)	2151	(71.1)
Mean body mass index	25.4	(4.5)	25.1	(4.3)
Current smoking	1415	(23.9)	788	(26.0)
Regular alcohol intake	4717	(80.0)	2514	(82.9)
Gyneacological status				
Hysterectomy and/or ovariectomy	1117	(18.9)	–	–
Use of HRT	826	(14.0)	320	(10.6)
Use of OAC	531	(9.0)	377	(12.4)
No use of estrogen/progesterone	4463	(75.6)	2332	(76.9)
Premenopause	982	(22.2)	513	(21.9)
Perimenopause	2276	(50.9)	1189	(51.0)
Postmenopause	1205	(26.9)	630	(27.1)

Table 2
Differences in mean scores on the menopausal self rating scale, its subscales and the EDS score, between women with hormone replacement therapy (HRT), oral contraceptives (OC) and non users (ANOVA)

	HRT users ($n=320$)		OC users ($n=377$)		Non users ($n=2332$)		F	P
Vasomotor scale								
Mean score (SD)	2.43	(2.81)	1.59	(2.21)*	2.33	(2.69)	11.02	<0.001
Urogenital scale								
Mean score (SD)	1.66	(2.21)	1.28	(1.97)	1.29	(2.01)	3.08	<0.04
Cognitive/Vegetative scale								
Mean score (SD)	15.30	(9.47)*	11.82	(9.13)	11.93	(9.28)	16.92	<0.001
EDS score								
Mean score (SD)	8.04	(6.13)*	6.58	(5.8)	6.38	(5.72)	10.73	<0.001

ysis was performed using the Scheffe procedure. The independent relationship of depressive symptoms to the intensity of menopausal complaints was assessed by multiple linear regression analysis, taking into account several other independent variables known from the literature to interfere with climacteric signs, such as age, body mass index, parity, educational level, employment, marital status, and current smoking habits.

3. Results

The EDS was highly correlated to the cognitive–vegetative subscale and to a lesser degree to the vasomotor and urogenital subscales (0.72, 0.41 and 0.37, respectively, two tailed $P < 0.001$).

Table 2 (ANOVA) shows the differences in mean scores on the menopausal self-rating subscales and the EDS between women using HRT or OC and non users. Women using HRT showed the highest scores on all subscales. In a post hoc analysis following the Scheffe procedure, on the EDS and the cognitive–vegetative subscale, the scores of the HRT users were significantly higher than the scores of those using OC and of those of non users. Moreover, OC users had significantly lower scores on the vasomotor subscale compared to HRT users and to non users. On the uro-genital subscale, HRT users had higher (although not significantly) scores than the OC users and the non users. The scores on the menopausal subscales in the different groups (HRT, OC and non users) were used as dependent variables for multiple linear regression analysis, with the EDS scores and several other variables being used as independent variables (Table 3). In all groups, the EDS scores contributed the most to the explained variance on the subscales. Of the non users, only postmenopausal status (no period for at least 12 months) proved to be a more important determinant of the variance of the scores on the vasomotor subscale.

4. Discussion

Although, during menopausal transition, women experience many somatic and emotional symptoms, no direct correlation with the declining estrogen production has ever been demonstrated [12]. Moreover, the overall lack of clear positive findings regarding any positive effect of HRT on emotional symptoms is disappointing [13,14]. It is known from clinical practice that women who present all kinds of complaints, may well be suffering from underlying depression. This paper examined the association between depression and the presentation of climacteric complaints.

Comparing cognitive and vegetative scores on a menopausal self-rating scale to scores on a depression self-rating scale (EDS) revealed a very high correlation (0.72), suggesting that symptoms which are commonly regarded as being 'typically' related to menopausal transition, actually reflect depressive symptomatology. If there is any relationship between declining estrogen production and these depressive symptoms, it might be hy-

Table 3
Multiple linear regression analysis with scores of climacteric complaints on the self rating questionnaire sub scales as dependent variable

Sample	A[a] ($n = 320$)				B[b] ($n = 377$)				C[c] ($n = 2332$)			
	Total scale	Vasomotor scale	Urogenital Scale	Cognitive vegetative scale	Total scale	Vasomotor scale	Uro genital scale	Cognitive vegetative scale	Total scale	Vasomotor scale	Uro-genital scale	Cognitive vegetative Scale
Adjusted R square	0.47	0.11	0.04	0.53	0.45	0.09	0.02	0.49	0.50	0.18	0.10	0.53
	Beta				Beta				Beta			
Age	0.04	0.03	0.07	0.02	0.05	0.06	0.07	0.03	0.01	0.03	−0.00	0.01
BMI	0.07*	0.16*	0.03	0.06	0.09*	0.15*	0.11	0.04	0.06*	0.09*	0.00	0.05*
Parity	−0.05	−0.05	−0.08	−0.03	−0.05	−0.07	−0.08	−0.02	−0.03	−0.03	−0.04	−0.02
EDS	0.67*	0.25*	0.22*	0.72*	0.66*	0.30*	0.14*	0.69*	0.65*	0.21*	0.26*	0.70*
Education level	−0.04	−0.11*	−0.01	−0.01	0.03	0.01	0.01	0.03	0.00	−0.07*	−0.02	0.03
Employment	−0.07	0.02	0.02	−0.08*	−0.08	0.05	−0.06	−0.01*	−0.07*	−0.04*	−0.00	−0.07*
Marital status	−0.07	−0.09	−0.11	−0.04	0.00	−0.03	0.00	0.01	−0.02	−0.04	−0.01*	0.00
Smoking	0.07	0.04	0.02	0.08	0.06	0.07	−0.04	0.06	0.06*	0.08*	−0.05*	0.06*
Menopause	–	–	–	–	–	–	–	–	0.15*	0.28*	0.17*	0.07*

[a] Women receiving HRT.
[b] Women receiving OAC.
[c] Women not receiving any estrogen.
* $P < 0.05$.

pothesised that women taking HRT should have lower scores on the EDS than non users. This was not the case in our study (Table 2): the highest scores on the EDS were recorded in HRT users. Subsequent multiple linear regression analysis (Table 3) with scores on the menopausal subscales as the dependent variable, showed that depressive symptomatology contributed most strongly to the explained variance within all groups. Moreover, in the non users, postmenopausal status usually contributed to high scores on the vasomotor subscale and, to a minor degree, on the uro-genital subscale, but almost never to high scores on the cognitive–vegetative subscale. This suggests that declining estrogen production is indeed associated with vasomotor symptoms, whereas it has hardly any effect on cognitive and vegetative symptoms.

As far as we know, this is the first study to investigate the correlation between depressive symptomatology and menopausal complaints (taking into account the effect of hormone substitution) in a cohort of women representatives, of the female population aged between 47 and 54 years.

What is the clinical relevance of these findings? Firstly, it might be suggested that, during menopausal transition, women with vasomotor symptoms, benefit from HRT, whereas the use of HRT for other 'emotional' symptoms is questionable. Secondly, and even more importantly, the general practitioner who is consulted by a woman presenting several complaints of other than of vasomotor origin, should realise that she might be suffering from underlying depression. This would hopefully lead to a more accurate diagnosis of depression and, as a consequence, to more appropriate treatment: counselling and/or the use of anti-depressants instead of a prescription for HRT.

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References

[1] Murray CJL, Lopez AD. The Global Burden of Disease. USA: Harvard School of Public Health on behalf of the World Health Organisation and the World Bank, 1995.

[2] Kind P, Sorensen J. The costs of depression. Int Clin Psychofarm 1993;7:191–5.

[3] Bijl RV, van Zessen G, Ravelli A. Psychiatric morbidity among adults in the Netherlands: the NEMESIS study: II: prevalence of psychiatric disorders. Ned Tijdschr Geneesk 1997;141:2453–60 (in Dutch).

[4] Ormel J, Koeter MW, Van den Brink W, Van de Willige G. Recognition, management and course of anxiety and depression in general practice. Arch Gen Psych 1991;48:700–6.

[5] Schwingl PJ, Hulka BS, Harlow SD. Risk factors for menopausal hot flashes. Obst Gyn 1994;84:29–34.

[6] Smeets Goevaers CG, Leusink GL, Papapoulos SE. The prevalence of low mineral denity in Dutch perimenopausal women: the Eindhoven perimenopausal osteoporosis study. Osteo Int 1998;8:404–9.

[7] Oldenhave A, Jaszman JB, Haspels AA, Everaerd WT. Impact of climacteric on well being. Am J Obst Gyn 1993;168:772–80.

[8] Hunter Myra. The south-east England longitudinal study of the climacteric and postmenopause. Maturitas 1992;14:117–26.

[9] Holte A, Mikkelsen A. The menopausal syndrome: a factor analytic replication. Maturitas 1991;13:193–203.

[10] Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. B J Psych 1987;150:782–6.

[11] Cox JL, Chapman G, Murray D, Jones P. Validation of the Edinburgh postnatal depression scale (EPDS) in non postnatal women. J Aff Dis 1996;39:185–9.

[12] Pearlstein TB. Hormones and depression: what are the facts about premenstrual syndrome, menopause and hormone replacement therapy? Am J Obst Gyn 1995;173:646–53.

[13] Pearce Jane, Hawton Keith, Blake Fiona. Psychological and sexual symptoms associated with the menopause and the effects of hormone replacement therapy. B J Psych 1995;167:163–73.

[14] Porter M, Penney GC, Russel E, Templeton A. A population based survey of women's experience of the menopause. B J Obst Gyn 1996;103:1025–8.

[15] Pop VJ, Maartens LW, Leusink GL, Weetman AP. Are auto-immune thyroid dysfunction and depression related? J Clin Endocrinol Metab 1998;83:3194–7.