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ORIGINAL ARTICLE

Hormonal therapy in menopausal transition: implications for improvement of health-related quality of life

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ABSTRACT

The study aim was to assess scores of the Menopause Rating Scale (MRS) among women who use and desire to use hormonal therapy (HT), as well as to evaluate factors contributing to HT use and desire to use HT among women in menopausal transition. A total of 513 mid-aged women participated in the study. Data were collected using socio-demographic questionnaire, MRS and Beck Depression Inventory. The prevalence of current HT use was 9.7%, while 4.5% of women who did not use HT expressed a desire to start using HT. The MRS cutoff score for HT use was 10.5 and 11.5 among those who desire to use HT. Living in the central city districts, having lower body mass index, younger age at menopause, more gynecological illnesses, and worse MRS were associated with HT use. Living in the central city districts, having fewer births, more gynecological and chronic illnesses and having more depressive symptoms were associated with the desire to use HT. Mid-aged women who perceive their quality of life as poor due to climacteric symptoms should be advised to consider HT to improve their health status and everyday functioning.

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Menopause; hormone therapy; symptoms; women's health

Introduction

Hormonal replacement therapy (HT) has often been used in the treatment of climacteric symptoms [1]. The intensity of climacteric symptoms plays an important role in deciding whether to use the HT. A recent study suggested that the highest score (equivalent of very severe intensity) for any of the symptoms listed in the Menopause Rating Scale (MRS) should be indicative of HT adoption [2]. However, data on MRS score cutoffs for HT use are lacking in the Caucasian population.

The MRS is widely used to examine the level of bothersome menopausal symptoms both among perimenopausal and postmenopausal women [3]. It is a brief questionnaire, composed of only 11 items, that allows practitioners rapid orientation as to the specific problems affecting woman's health-related quality of life (HRQoL) [4]. Next, this scale considers 3 major disturbances during menopausal transition (mental, somatic, and urogenital) that can be examined independently as well as a whole. Scoring of MRS is relatively easy because it does not require reverse scoring or other mathematical procedures, but rather simple adding up of each item score that can be performed without a calculator. Finally, MRS has been validated as the outcome measure of HT use [5,6].

Previous studies reported that women who were more affluent, had higher education level, lived in urban areas, had lower body mass index (BMI) and parity and who smoked were more likely to use HT in postmenopause [7–10]. However, limited data are available on characteristics of women who have not previously been using HT but wish to use HT in the future.

The study's aim was to assess scores of the MRS among women who use and do not use HT as well as among women who wish to use HT and those who do not. In addition, the study aimed at evaluating factors contributing to use and desire to use HT among peri- and post-menopausal women.

Methods

Peri- and postmenopausal women who were scheduled for annual gynecological checkups from February 2014 to January 2015 in the primary health care setting were invited to participate in this study. Out of the existing 17 Community Health Centers (CHC) in Serbian capital city Belgrade, we randomly selected two (one in the central and one in the suburban district) for study recruitment. Women in CHC were of diverse backgrounds, which allowed us to include different socio-demographic aspects in this analysis. The study was approved by the Institutional Review Boards of the corresponding CHCs ('Palilula' and 'Zemun'). All women signed informed consent for participation.

The inclusion criteria were being 40–65 years old, speaking the Serbian language, and providing signed informed consent. The exclusion criteria were: confirmed psychiatric diseases, malignancies, or acute deterioration of a debilitating illness, filling in less than 90% of survey and not fulfilling the inclusion criteria. Menopausal status was ascertained according to last menstrual period and other data regarding menstrual cycle and symptoms (STRAW + 10 principal and descriptive criteria) [11].

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Supplemental data for this article can be accessed here.

Mid-aged women experiencing climacteric symptoms with regular or irregular menstrual cycles were labeled as perimenopausal.

Instruments

Socio-demographic questionnaire included age, district of residency, level of education, employment status, marital status, and household income. Lifestyle items included smoking status, alcohol use, regular weekly recreation, physical activity (vigorous, moderate and sedentary), and work activity (vigorous, moderate and sedentary). Health-related items examined general medical history (BMI, chronic illnesses, use of medications) and gynecological history and use of HT, duration of HT use, and desire to use HT.

The MRS is a self-administered instrument covering 11 climacteric symptoms or complaints experienced in menopausal transition [4]. Symptoms are combined into three independent domains: psychological (PD), somato-vegetative (SVD) and urogenital (UD). Items are rated on a 5-point Likert scale (no symptom – 0, very severe symptom – 5). The scoring is done by adding up the reported rating. The total score ranges between 0 (asymptomatic patient) and 44 (highest degree of complaints). Scores >7 for PD, >9 for the SVD, >4 for UD, and >17 for the total MRS have been used to define severe effects on HRQoL. The Serbian version of MRS has been previously validated [12].

Beck's Depression Inventory (BDI) is a one-dimensional scale with 21 items for assessment of depression symptoms, its severity, and impact on daily functioning [13]. Answers are graded on a four-point scale from 0 to 3. The total BDI score ranges from 0 to 63 and represents the sum of grades for each item with higher scores indicating more depressive symptoms. The BDI is one of the most commonly applied questionnaires to ascertain the presence of depression (BDI ≥21) in otherwise healthy population. The scale has been translated and validated in Serbian language [14]. Previous studies reported association of depressive symptoms with poorer HRQOL [15]. Similarly, studies among perimenopausal women documented presence of depressive symptoms, while some women during menopausal transition, in fact, may develop more severe forms of depression [16]. Moreover, literature data indicate that use of HT may alleviate symptoms of menopausal depression [16]. Because of this, precise consideration of depressive symptoms in this study is important, due to its potential confounding effect in the association between use of HT and the level of HRQoL.

Statistical analysis

ANOVA (parametric and non-parametric Kruskal–Wallis χ^2 test) was used to investigate differences in participants' characteristics, BDI and MRS scores. Spearman's correlation investigated the relationships between the observed parameters and MRS scores, HT use, duration of HT use and desire to use HT. Receiver Operating Characteristics (ROC) analysis was performed to test the reliability of the BDI and MRS scores for prediction of HT use and a desire to use HT and to set the cutoff levels of these scores above which mid-aged women should be suggested to take HT for potential HRQoL improvement. The ROC analysis was performed to evaluate the period of HT use after which improvement in HRQoL could be noticed. Binary logistic regression analysis (Enter and Forward Wald methods) was applied to assess factors associated with HT use and desire to start using HT. The independent variables were women's socio-demographic, lifestyle, general medical, and gynecological history data registered through the general questionnaire as well as BDI and MRS scores. Statistical Package for Social Sciences (SPSS) version 20.0 (SPSS Inc., Chicago, IL) was used in data analysis.

Results

This study sample comprised 513 mid-aged women out of which 50 (9.7%) reported using HT. All women who already used HT expressed a desire to continue using HT. Additionally, there were 21 (4.5%) women who did not currently use HT but were interested to start using HT. The average duration of HT use was 36.0 4 ± 27.58 months (range from 5 to 125 months). Significantly more postmenopausal women used HT while only five perimenopausal women had already started HT use. Contrary, a similar proportion of women were and were not interested in HT use regardless of their menopausal status.

Socio-demographic and behavioral characteristics of women are presented in Tables 1 and 2. There were no significant differences between women who used/wanted HT and did not use/want HT. Almost all parameters were similar among women who used HT and those who desired to use HT. Correlations of the observed parameters with use and desire to use HT as well as the MRS total score are shown in Supplemental Table S1.

Upon confirming numerous significant associations of HRQoL with HT use, the ROC analysis was performed to set the cutoff levels of MRS above which our mid-aged women should be suggested to take HT for HRQoL improvement (Table 3; Supplemental Figure S1). For postmenopausal women suggested MRS cutoff score was 10.5. Women in menopausal transition who did not take HT and had MRS > 11.5 and BDI > 8.5 felt that they needed HT.

Women who reported longer use of HT had better psychological, somato-vegetative, and overall HRQoL in menopausal transition (Table 2). Therefore, we performed the ROC analysis to investigate the duration of HT after which a significant improvement of HRQoL could be noticed. The proposed cutoff time was 44 months (Table 3; Supplemental Figure S2).

Factors associated with HT use were living in central city districts, having lower BMI, younger age at menopause, more gynecological illnesses and worse HRQoL ($B = -1.747$; Wald = 119.602; Nagelkerke $R^2 = 0.622$; $\chi^2 = 49.980$; $p = .001$; explained variance = 87.7%). Factors associated with the desire to use HT were living in central city districts, having fewer births, more gynecological and chronic illnesses and having more depressive symptoms ($B = -2.061$; Wald = 131.939; Nagelkerke $R^2 = 0.721$; $\chi^2 = 45.653$; $p = .001$; explained variance = 89.7%).

$$\begin{aligned}\text{HT use} = {} & 6.947 - 0.968 \times \text{city district} - 0.153 \times \text{BMI} - 0.142 \\ & \times \text{menopause age} + 2.273 \times \text{gynecological illnesses} \\ & + 0.067 \times \text{MRS}\end{aligned}$$

$$\begin{aligned}\text{HT desire} = {} & 2.874 - 1.138 \times \text{city district} - 0.621 \\ & \times \text{number of births} - 0.093 \times \text{menopause age} \\ & + 0.394 \times \text{chronic illnesses} + 1.698 \\ & \times \text{gynecological illnesses} + 0.051 \times \text{BDI}\end{aligned}$$

Discussion

This study found that 9.7% of the investigated Serbian women used HT, while another 4.5% of women expressed the desire to start using HT. This prevalence is lower than the estimated 16% HT use in Europe [17]. However, the prevalence of HT found in

Table 1. Differences in frequency (KW χ^2) of women who use/want and do not use/want hormone therapy regarding socio-demographic characteristics and quality of life.

Parameters	Does not use HT	Uses HT	*p*	Does not want HT	Wants HT	*p*
Desire to use start with HT						
No	442	0	**.001**	/	/	/
Yes	21	50		/	/	
Menopausal status						
Peri	188	5	**.005**	178	25	.250
Post	275	45		264	46	
Menstrual cycle						
Regular	438	39	**.001**	417	60	**.006**
Not regular	25	11		25	11	
Residency district						
City center	227	35	**.003**	212	50	**.001**
Outskirts	236	15		230	21	
Marital status						
Married/coupled	54	11	**.037**	52	13	.093
Other	409	39		390	58	
Education						
No/primary $\leq$8	50	5	.396	48	7	.316
Secondary	227	20		218	29	
Higher $\geq$12 years	186	25		176	35	
Employment						
No	215	15	**.018**	208	22	**.008**
Yes	248	35		234	49	
Smoking						
Smoker	151	14	.798	137	28	.326
Former smoker	98	11		97	12	
Non*smoker	214	25		208	31	
Alcohol use						
No	352	35	.219	337	50	.181
Yes	111	15		105	21	
Alcohol frequency						
Every day	3	0	.756	2	1	.515
Weekly	24	2		24	2	
Monthly	33	4		30	7	
Rarely	55	9		53	11	
Recreation						
No or rarely	122	11	.316	113	20	.369
Regularly	341	39		329	51	
Physical activity						
Very hard	29	4	.893	29	4	.415
Energetic	85	9		77	17	
Moderate	349	37		336	50	
Work activity						
Hard	62	15	**.006**	59	18	**.029**
Average	234	18		220	32	
Sitting/standing	167	17		163	21	
Chronic illnesses						
No illness	148	12	**.005**	142	18	.157
Chronic illnesses	315	38		300	53	
Gynecological illnesses						
No	114	2	**.001**	109	7	**.003**
Yes	349	48		333	64	
Climacteric symptoms						
No symptoms	83	2	**.005**	83	2	**.001**
Has symptoms	380	48		359	69	
BDI category						
No depression	441	40	**.001**	423	58	**.001**
Depression	22	10		19	13	
PD categories						
Below 7 – good	364	31	**.009**	349	46	**.008**
Above 7 – poor	99	19		93	25	
SVG categories						
Below 9 – good	437	40	**.001**	418	59	**.002**
Above 9 – poor	26	10		24	12	
UD categories						
Below 4 – good	375	39	.364	361	53	.111
Above 4 – poor	88	11		81	18	
MRS categories						
Below 17 – good	371	34	**.039**	357	48	**.011**
Above 17 – poor	92	16		85	23	

Bold values denote statistical significance. PD: psychological domain; SVG: somato-vegetative domain; UD: urogenital domain; MRS: menopause rating scale.

Table 2. Differences (ANOVA F) in tested parameters between women regarding HT use and duration.

	Mean	Standard deviation	Mean	Standard deviation	
Parameters	Does not use HT		Uses HT		*p*
Women's age	51.25	6.31	51.71	5.66	.631
BMI (Body Mass index)	26.10	8.51	23.97	3.24	.079
Salary in Euros	516.08	349.21	497.97	277.95	.723
Smoking duration in years	20.61	9.42	20.16	8.83	.818
Number of cigarettes per day	16.20	7.81	15.39	12.39	.655
Age of menarche	13.31	1.66	13.26	1.77	.811
Number of pregnancies	2.62	1.87	2.34	1.45	.300
Number of live births	1.64	0.79	1.36	0.80	**.016**
Number of miscarriages.	0.30	0.73	0.41	1.06	.427
Number of induced abortions	0.89	1.57	0.44	0.86	**.044**
Age at menopause	49.04	4.18	46.91	3.9	**.005**
Psychological domain score	4.22	3.66	6.06	4.71	**.001**
Somato-vegetative domain score	4.05	3.07	5.78	3.55	**.001**
Urogenital domain score	2.27	2.45	3.08	3.02	**.031**
MRS total score	10.55	7.82	14.92	9.88	**.001**
BDI total score	6.38	7.47	11.26	12.92	**.001**
Parameters	Does not want HT		Wants to start with HT		*p*
Women's age	51.18	6.37	52.01	5.41	.307
BMI (Body Mass index)	26.14	8.67	24.35	3.42	.086
Salary in Euros	514.72	351.43	511.83	284.77	.947
Smoking duration in years	20.61	9.55	20.41	8.25	.901
Number of cigarettes per day	16.19	7.81	15.76	10.75	.768
Age of menarche	13.27	1.57	13.57	2.18	.152
Number of pregnancies	2.66	1.89	2.18	1.38	**.042**
Number of live births	1.65	0.78	1.36	0.81	**.004**
Number of miscarriages.	0.31	0.73	0.35	0.95	.686
Number of induced abortions	0.92	1.61	0.39	0.81	**.006**
Age at menopause	49.06	4.11	47.31	4.44	**.008**
Psychological domain score	4.21	3.65	5.64	4.51	**.003**
Somato-vegetative domain score	4.01	3.09	5.56	3.31	**.001**
Urogenital domain score	2.21	2.41	3.16	2.99	**.003**
MRS total score	10.43	7.79	14.38	9.38	**.001**
BDI total score	6.23	7.21	10.77	12.42	**.001**
	HT duration				*p*
Psychological domain score					**.024**
Somato-vegetative domain score					**.047**
Urogenital domain score					.264
MRS total score					**.045**
BDI total score					.742

Bold values denote statistical significance. MRS: menopause rating scale; BDI: Beck Depression Inventory; HT: hormone therapy.

Table 3. ROC analysis of cutoff Menopause Rating Scale scores (for three domains and total score) suggested for HT use in order to improve quality of life.

Parameters	Explained % of cases	*p*	Cutoff value	Sensitivity %	Specificity %
Use of HT in postmenopausal women					
PD	64.2	.006	5.5	51.4	65.1
SVG	66.0	.002	4.5	62.9	58.5
UD	61.1	.032	3.5	51.4	68.0
MRS total	65.4	.003	10.5	60.1	53.1
BDI total	60.8	.037	8.5	45.7	68.4
Desire to use HT total sample of mid-aged women					
PD	58.7	.018	4.5	54.3	55.3
SVG	62.9	.001	4.5	60.9	59.1
UD	59.7	.009	3.5	52.2	68.9
MRS total	61.9	.001	11.5	54.3	58.3
BDI total	60.0	.007	8.5	41.3	68.2
HT use duration in months					
PD categories	71.2	.012	44.0	57.9	77.4
SVG categories	69.0	.065	44.0	70.0	74.3
UD categories	64.5	.146	44.0	63.6	71.8
MRS categories	74.4	.006	44.0	68.8	79.4
BDI categories	73.1	.025	44.0	70.0	72.5

PD: psychological domain; SVG: somato-vegetative domain; UD: urogenital domain; MRS: menopause rating scale; BDI: Beck Depression Inventory; HT: hormone therapy.

this study is higher compared to HT use among women in Sweden or Italy, where the frequency of HT use of 6% and 4% respectively, were reported [18,19].

Suggested MRS cutoff score for HT use and desire to use HT in this study considered relatively balanced levels of sensitivity and specificity, without having larger discrepancies between the two values. The BDI and MRS scores were reliable for the prediction of HT use. The cutoff MRS that was deemed appropriate for use of HT in our sample of women was 3.5 points lower than previously observed among women in Chile (10.5 versus 14) [2]. These findings suggest that perception of menopausal symptoms varies across cultures as a subjective sense of disturbances can be perceived differently regardless of the MRS score.

It has been observed that the use of HT in menopausal transition has decreased over the past two decades [20] due to evidence from the Women's Health Initiative study suggesting that HT users are at risk of developing breast cancer [21]. However, it is still considered that not enough women are sufficiently informed about the benefits and potential risk of HT use in menopausal transition [19]. Because of this and taking into consideration the MRS cutoff scores observed in our study, it is recommended that all women in menopausal transition are tested using MRS. Based on the obtained scores further discussion and

HT counseling in women's health services should ensue. Assessment of menopausal symptoms might not be a routine practice in some settings due to the lack of recognition either by lay public and/or medical professionals. However, possibility for HT use should be offered to all women who score above the MRS cutoffs. In this way, MRS could become a potential screening procedure during regular gynecological checkups for HT use.

Factors associated with the use of HT in this study are congruent with previous studies in terms of living in urban areas and BMI [7,8]. Women living in urbanized areas might have more possibilities to consult different health services that could facilitate a decision to start using HT. The level of education and behavioral patterns that were observed in other European populations [7,8,10] were not indicative of HT use, suggesting that clinical and demographic factors play more important role in HT use in Serbia. Having gynecological illnesses in menopausal transition might contribute to having more intense somatic symptoms, which in turn impair everyday functioning.

Women who intend to use HT are more likely to believe that benefits to HT use are greater than risks [22] as well as that HT would improve their physical and mental health and the overall well-being [23]. In our study sample, women who expressed the desire to start using HT shared some characteristics with women who were already using HT, such as living in central city districts, were younger and had gynecological illnesses. Living in central districts could be regarded as proxy of being more aware of HT and having easier access to HT, compared to women living in suburban areas. However, these women were more likely to have other chronic illnesses and more depressive symptoms. Interestingly, women who desired to use HT did not have as intense menopausal symptoms and impaired HRQoL as measured by the MRS. Contrary, limitations and impairment due to physical and mental health seem to play a role in desire to use HT in our sample of mid-aged women.

Several limitations of this study should be considered. We recruited women during their annual gynecological checkup which are not mandatory by law. Therefore, women from our sample might be more health conscious than others. Because investigated women lived in the largest urban area in the country, our results may be limited to other urbanized female populations, while specific features of women from rural areas are yet to be analyzed. Our results are also limited by a cross-sectional study design, which precludes inference, but captures the assumptions of associations between variables. Future studies on HT and MRS should include long-term follow-up of menopausal women. In this way, women who score above the MRS cutoff for HT use could start with therapy and be compared to those who score below the MRS cutoff for HT use and who remain without HT. Moreover, women who opt for HT use could be compared to women who opt not to use HT. During the follow-up women could be tested with MRS regularly to follow the symptoms dynamics in time, along with the standard gynecological examination and behavioral questionnaire. For women who have chronic illnesses changes in treatment should be examined relative to menopausal symptoms. This information could be used to assess whether HT is needed/wanted over yearly intervals.

In conclusion, women who had more severe menopausal symptoms used HT, while women who had worse physical and mental health desired to start using HT. Mid-aged women who perceive their HRQoL as poor due to climacteric symptoms should be advised to consider HT to improve their health status and everyday functioning.

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Disclosure statement

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