



Attitudes to the prescription of menopause hormone therapy for vasomotor symptoms and osteoporosis for patients of different ages: A survey of gynecologists in Belgium

Serge Rozenberg*, Jean Vandromme

Department of Obstetrics and Gynecology, CHU St Pierre, Laboratoire de santé génésique ULB, Brussels, Belgium

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ABSTRACT

Introduction: The interpretation of the literature on menopause hormone therapy (MHT) has evolved enormously over the last decade. In recent years, guidelines have reinstated the place of MHT.

Aim: This survey analyzes the prescription (initiation and maintenance) of MHT in relation to patient age and therapy indications.

Material and method: Two vignettes were sent to gynecologists working in Belgium in a random survey. One vignette concerned the initiation of therapy for a woman who was either 52 or 62 years old, suffering either from severe vasomotor symptoms (VSM) or from osteoporosis. The second vignette concerned the maintenance of MHT or switching to another medication in a woman aged 62 years who suffered either from VSM (when stopping MHT) or from osteoporosis. The physicians were asked how they would treat these two patients.

Results: We analyzed 443 vignettes from 222 physicians.

Initiation of MHT: 84% of the respondents would initiate MHT for a 52-year-old woman with VMS, whereas only 32% would do so for a 52-year-old woman who had osteoporosis (chi square = 33; $p < 0.001$). 51% would initiate MHT for a 62-year-old woman with VMS, whereas only 14% would do so for a 62-year-old woman with osteoporosis (chi square = 17; $p < 0.001$).

Maintenance of therapy: 87% would maintain MHT for a 62-year-old woman with severe VMS and 52% would do so for a 62-year-old woman with osteoporosis (Chi Square 31; $p < 0.001$).

Conclusion: VMS are recognized as an indication for MHT, but osteoporosis much less so, even for women around the age of 50.

1. Introduction

The use of menopause hormone therapy (MHT) has decreased dramatically in all countries since the initial findings of the Women's Health Initiative (WHI) were published in 2002 [1]. Physicians' advice and women's decisions regarding MHT have been clouded by anxiety and confusion for the past decade [2]. Moreover, a generation of physicians has not been adequately trained in menopause management [2,3].

However, the interpretation of the literature on MHT, including the WHI results, has evolved enormously over the last decade [2,4], and in recent years guidelines and opinion papers in leading journals have reinstated its place in the management of menopause. [2,5–7]. Discrepancies may therefore exist between scientific societies' guidelines and physicians' attitudes and opinions.

The aim of this study was to analyze how the medical viewpoint of gynecologists regarding MHT varies according to demographic and clinical variables, specifically patient age, and the indications, namely the presence of severe vasomotor symptoms (VMS) or osteoporosis, in the absence of a contraindication to MHT. Their viewpoints could then be compared with the current recommendations from scientific societies [5–7]. We chose to analyze both the initiation and the maintenance of MHT in this context.

2. Material and method

2.1. Survey: case construction

2.1.1. Initiation of MHT

To answer the question of whether MHT would be prescribed for

* Corresponding author.

E-mail address: serge_rozenberg@stpierre-bru.be (S. Rozenberg).

VMS and or osteoporosis, we used case scenarios [8]. We started with a case scenario of a Caucasian postmenopausal woman whose menopause had occurred at the age of 50. She had no significant personal or family history, in particular no risk factors for cardiovascular disease or breast cancer (normal BMI, gynecological examination, mammography and laboratory results). We then modified this case by [1] changing her age (52 or 62 years old) [2], considering that she presented very severe persistent VMS but a normal bone mineral density (BMD) result, or [3] considering that she had no VMS but did have severe osteoporosis (T score = -2.9 both at vertebrae and femur, with respectively a 10-year Frax risk for all osteoporotic fractures of 5.6% at age 52 and 11% at age 62, and for hip fracture of 0.8% at age 52 and 2.1% at age 62). We added that the patient's mother had osteoporosis. Only one of these four case scenarios was sent to each gynecologist in a survey (see below), who was asked to state what treatment he or she would prescribe.

2.1.2. Maintenance of MHT

Similarly, we submitted a case of a 62-year-old patient who used MHT. She had no significant personal or family history, in particular no risk factors for cardiovascular disease or breast cancer (normal BMI, gynecological examination, mammography and laboratory results). Here we modified the case in the following ways [1]. In one case, MHT was prescribed for severe VMS, which would recur if MHT was stopped. In this case scenario, the BMD was normal [2]. In the next case scenario, there was no mention of VMS, but the patient had osteoporosis (T score = -2.9 both at vertebrae and femur, with a 10-year Frax risk for all osteoporotic fractures of 11% and for hip fracture of 2.1%). In neither of these cases did we mention whether BMD had changed over time. Again, though, we did mention that the patient's mother had suffered from osteoporosis. Likewise, only one case scenario from this category was sent to each gynecologist, who was then asked which treatment he or she would prescribe.

2.1.3. Outcomes

The main outcome was whether or not the gynecologist would prescribe (initiate or maintain) MHT.

2.1.4. Prescribed treatments

Physicians could prescribe more than one treatment, which might be MHT, non-hormonal treatment, complementary and alternative medicine (CAM) (such as pollen extract, phytoestrogens), non-hormonal medication (such as an SSRI, gabapentin, clonidine), calcium and vitamin D, a selective estrogen receptor modulator, a bisphosphonate, denosumab or other.

2.1.5. Survey

A request to participate in our survey was sent by email to a list of gynecologists working in Belgium, derived from various lists held by gynecologist associations (1973 email addresses for over 1000 active gynecologists). A first email was sent on 11.1.19 and a reminder on 12.3.19. In order to be in accordance with the General Data Protection Regulation (GDPR), only those physicians who agreed to respond to the survey were sent it. The physicians were assured that their responses would remain anonymous and that the survey was not commercially motivated. Those who agreed were directed to a Monkey survey link, which included two cases, at random (one from the initiation cases and one from the maintenance cases). A questionnaire requesting demographic data was included. In total, 222 physicians responded to the survey.

This study was approved by the internal review board of our institution.

2.2. Statistical analysis

2.2.1. Sample calculation

We estimated that the survey would be sent to 1000 gynecologists.

We knew from similar surveys that a number of gynecologists are not interested in the subject (such as obstetricians, ART and fetal medicine specialists) and our hope was to obtain a response rate of 25%, which would be a total of 250 analyzable responses, with at least 40–50 answers per vignette. We calculated a sensitivity analysis for the survey. Assuming, for instance, that 90% of the physicians would initiate MHT for a severely symptomatic 52-year-old woman in early postmenopause but only 50% would do so for a 62-year-old woman, nearly 46 cases would be needed to find a significant difference with a power of 80% and a type I error (alpha) of 5%. Similarly, assuming that 50% of gynecologists would maintain MHT for a 62-year-old woman whose menopause began 10 years earlier but who still had severe symptoms and only 10% would maintain it for a similar patient with no symptoms, again, about 46 cases would be needed to show a significant difference ($p < 0.05$, power 80%). All analyses were performed using SPSS software. The effect of each of the factors on prescription rates was assessed using chi-square tests (univariate analyses). The significance level was set at $p < 0.05$. The study was approved by the local ethical committee.

3. Results

After the two emails, we obtained responses from 222 physicians, which represents about 20% of all Belgian gynecologists, and a total of 443 vignettes (222 concerning the initiation of MHT and 221 concerning the maintenance of MHT). The mean age \pm SD of the respondents was 51 ± 15 years; 57% were women and 43% men.

3.1. Initiation of menopause hormone therapy

The physicians' attitudes towards MHT prescription were significantly related to the case type. Eighty-four percent of gynecologists would initiate MHT for a 52-year-old woman with VMS and no osteoporosis, whereas 32% would do so for a 52-year-old woman with osteoporosis but no VMS (chi square = 33; $p < 0.001$). Fifty-one percent would initiate MHT for a 62-year-old woman with VMS and no osteoporosis, whereas only 14% would do so for a 62-year-old woman with osteoporosis but no VMS (chi square = 17; $p < 0.001$). The effects of age on MHT initiation for VMS (chi square = 13; $p < 0.001$) and on osteoporosis medication prescription (chi square = 6; $p < 0.02$) are also significant. The results for other treatments are presented in Table 1.

3.2. Maintenance of therapy

Eighty-seven percent of gynecologists would maintain MHT for a 62-year-old woman with severe VMS and no osteoporosis, and 52% would do so for a 62-year-old woman with osteoporosis (chi square 31; $p < 0.001$). The results for the other treatments are presented in Table 2.

4. Discussion

4.1. Initiation of MHT

Although there is no reason *not* to prescribe MHT to a 52-year-old woman with severe VMS and no contraindication for MHT, only about 85% of gynecologists would do so. That means that 15% would not have prescribed MHT as a first-choice treatment. Moreover, only about half of the surveyed gynecologists considered MHT to be a first-choice therapy for a similar patient aged 62 years.

During the late stages of the menopausal transition, almost three-quarters of women report moderate to severe VMS, and some women experience these for a decade or longer [2,9]. As these symptoms may cause sleep loss and reduced concentration, they may result in poor performance and even increased healthcare costs [10,11]. Systematic

Table 1
Number of initiated treatments (%) for four case scenarios (more than one treatment could be prescribed).

	52 years with severe VMS, normal BMD (n = 67)	52 years, osteoporosis, no VMS (n = 53)	62 years with severe VMS, normal BMD (n = 43)	62 years, osteoporosis, no VMS (n = 59)
MHT	56 (83.6%)	17 (32.1%)	22 (51.2%)	8 (13.6%)
CAM	13 (19.3%)	0	14 (32.6%)	0
Non-hormonal medication	1 (1.5%)	0	7 (16.3%)	0
Ca + vit D	23 (34.3%)	40 (75.5%)	17 (39.5)	48 (81.4%)
SERM	0	5 (9.4%)	1 (2.3%)	4 (6.8%)
Biphosphonates	1 (1.5%)	25 (47.2%)	0	30 (50.8%)
Denosumab	0	0	0	3 (5.1%)

MHT, menopause hormone therapy; CAM, complementary and alternative medicine; SERM, selective estrogen receptor modulators; VMS, vasomotor symptoms; BMD, bone mineral density. More than one treatment could be prescribed. Prescription rates of MHT are significantly different between the four case scenarios ($p < 0.001$).

Table 2
Maintenance of MHT and initiation of treatment (%) for two case scenarios of women using MHT (more than one treatment could be prescribed).

	62 years, with VMS, normal BMD (n = 114)	62 years, osteoporosis, no VMS (n = 107)
MHT	99 (86.8%)	56 (52.3%)
CAM	10 (8.8%)	2 (1.9%)
Non-hormonal medication	3 (2.6%)	1 (0.9%)
Ca + vit D	46 (40.4%)	61 (57.0%)
SERM	1 (0.9%)	4 (3.7%)
Biphosphonates	0	69 (64.5%)
Denosumab	0	14 (13.1%)

MHT, menopause hormone therapy; CAM, complementary and alternative medicine; SERM, selective estrogen receptor modulators; VMS, vasomotor symptoms; BMD, bone mineral density. More than one treatment could be prescribed. Prescription rates of MHT are significantly different between the two case scenarios ($p < 0.001$).

reviews and meta-analyses of randomized controlled trials have shown that systemic MHT is the most effective treatment for VMS, decreasing them by as much as 80% in frequency and 90% in severity compared with placebo [12]. Not surprisingly, medical societies devoted to menopausal care, such as EMAS, NAMS and IMS, agree that MHT is the most effective treatment available and should be recommended for women suffering from VMS, in the absence of contraindications (mainly elevated risk of breast cancer, stroke deep venous thrombosis or emboli) (5–7). This means that for the 52-year-old woman portrayed in our survey, with severe VMS, a consensus has emerged that the benefits of MHT likely outweigh the risks [2,5–7,9]. Our result is markedly different from that observed in a study conducted by Kling et al [3], in which 34% of surveyed postgraduates indicated that they would not offer MHT to a symptomatic, newly menopausal woman without contraindications [3].

Similarly, the 62-year-old woman portrayed in our survey could benefit from MHT since she had no co-morbidities contraindicating MHT, but only half of the surveyed physicians would have prescribed MHT for her. This can be explained by the fact that many publications and guidelines, such as the Endocrine Society guidelines, suggest that MHT, when prescribed, should be initiated before the age of 60, or within the first 10 years of menopause [5].

One question that is often asked is whether MHT should be discontinued after a few years of treatment. In this survey almost 90% of gynecologists would not stop prescribing MHT to a 62-year-old woman who needs it for VMS and who does not have contraindications to MHT. Both the North American Menopause Society and the American College of Obstetrics and Gynecology agree that the use of MHT should be individualized and not discontinued solely based upon patient age [6,13]. They suggest that extended use of MHT (beyond age 60 or even 65) may be acceptable when the clinician and the patient agree that the benefits

of symptom relief outweigh the risks [6,13]. The prevalence and persistence of VMS vary between studies and cultures, but VMS has been reported in up to 60% of patients, and even in many women aged 60 to 65. VMS can impair sleep and quality of life [14–16]. About a third of gynecologists would have prescribed MHT to treat osteoporosis in a 52-year-old woman and 13 percent would in a 62-year-old patient, whereas 50 and 64 percent respectively would have initiated other osteoporosis treatments, such as a biphosphonates, a selective estrogen receptor modulator (SERM) or denosumab, while 75 and 85 percent respectively would have prescribed calcium and vitamin D to these women. Similarly half of the surveyed gynecologists would discontinue MHT in cases of osteoporosis in the absence of VMS in a 62-year-old woman. They would, however, prescribe other medication, generally calcium and vitamin D (60%) and bisphosphonates, a SERM or denosumab (totaling 80%). Old guidelines considered that MHT prevented bone loss and recommended it [9], but more recent guidelines for treating osteoporosis, developed by endocrine or osteoporosis societies, recognize that MHT reduces vertebral, non-vertebral and hip fractures in postmenopausal women, and even in those women who have not been selected on the basis of low bone density or high fracture risk [17]. But because MHT has an unfavorable risk-benefit balance in older women, due to an increased risk of breast cancer and stroke, they restrict the use of MHT to osteoporosis, to younger postmenopausal women who are at high risk of fracture and who also have menopause symptoms [5,17]. Guidelines of the NAMS, endorsed by many gynecology and menopause societies, recognize that when alternate osteoporosis therapies are not appropriate or cause adverse events, the extended use of MHT is an option for women at high risk of osteoporosis [6]. It is therefore understandable that most physicians would consider the initiation of, or switch from MHT to, another osteoporosis treatment, such as calcium vitamin D and bisphosphonates, for a 62-year-old woman with osteoporosis.

This study is hampered by a number of limitations and possible biases. It is likely that the surveyed Belgian gynecologists are not representative of gynecologists living in other countries, since, for instance, the prescription and reimbursement conditions may vary between countries. Moreover, the gynecologists who answered the survey were probably those who are interested in the menopause. Based on the age distribution of the physicians who responded, we can estimate that about 60% of them had been trained before the WHI era.

Furthermore, only six vignettes were submitted. Complex clinical situations of patients with relative contraindications to MHT were not submitted, nor were vignettes of patients who had been hysterectomized and who would have needed estrogen-only therapy.

Finally, the results of the study were obtained through a survey and not in an actual clinical setting, in which patients interact with physicians and hopefully share in the decision making.

Nevertheless, this survey also presents some strengths. A large number of physicians took part in the survey, which was a randomized one. This methodology allowed us to modify a few parameters and

study their impact on the prescription rates of physicians. As expected, we observed that the presence of VMS was the strongest indication for MHT, since almost 85% of gynecologists would initiate MHT for a 52-year-old woman with severe VMS and no contraindication to therapy. This rate dropped to about 50% when the woman was 62-years-old, but about 85% would maintain the treatment if she was already using MHT. Only a third of gynecologists would initiate MHT for osteoporosis in a 52-year-old woman and this rate dropped to 14% for a patient aged 62 years, although about half of the surveyed gynecologists would maintain MHT for osteoporosis in a 62-year-old woman who was already using it.

Contributors

Serge Rozenberg designed of the study, did the analysis and wrote the first draft of the manuscript.

Jean Vandromme designed the survey, collected the data and revised the manuscript.

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Ethical approval

This study was approved by the local review board.

Provenance and peer review

Peer review was directed by Prof Margaret Rees independently of Serge Rozenberg (one of the authors and an Editor of *Maturitas*), who was blinded to the process.

Research data (data sharing and collaboration)

We agree to share appropriately anonymized data files from this research with other qualified professionals on request in order to confirm the substantive conclusions of the research, in fulfilment of APA Ethics Code Standard 8.14.

Declaration of Competing Interest

The authors declare that they have no conflict of interest.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:<https://doi.org/10.1016/j.maturitas.2019.07.024>.

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