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Women's experiences of menopause in an online MS cohort: A case series

R. Bove, M.D., M.Sc.[1,2,3], **T. Vaughan, Ph.D.**[4], **T. Chitnis, MD**[1,2,3], **P. Wicks, Ph.D.**[4], and **P. L. De Jager, M.D., Ph.D.**[1,2,3]

R. Bove: rbove@partners.org; T. Vaughan: tvaughan@patientslikeme.com; T. Chitnis: tchitnis@rics.bwh.harvard.edu; P. Wicks: pwicks@patientslikeme.com; P. L. De Jager: pdejager@rics.bwh.harvard.edu

[1]Partners Multiple Sclerosis Center, Department of Neurology, Brigham and Women's, Hospital, Brookline, MA 02445

[2]Harvard Medical School, Boston, MA 02115

[3]Center for Neurologic Diseases, Harvard Medical School, 77 Avenue Louis Pasteur, NRB168, Boston, MA 02115, USA

[4]PatientsLikeMe, Inc., Cambridge, MA, USA

Abstract

BACKGROUND—Many women with multiple sclerosis (MS) are postmenopausal. Previously reported findings from an online MS cohort suggested that earlier, surgical menopause may be associated with higher patient-reported MS severity scores.

OBJECTIVE—To explore experiences of menopause in a series of MS women responding to a reproductive survey from an online research platform, PatientsLikeMe (PLM).

METHODS—The free-text responses from a detailed reproductive history survey deployed to PLM members were analyzed using grounded theory approach.

RESULTS—Of the 208 free text responses, 127 responses related to menopause. Five themes emerged: (1) perimenopausal onset of MS symptoms, (2) overlap of MS and menopausal symptoms, (3) MS exacerbations and pseudo-exacerbations triggered by hot flashes, (4) escalation of disease course after menopause, including increasing fatigue, cognitive disturbance, and other

Corresponding Author: Riley Bove, MD, MSc, Brigham & Women's Hospital, Partners Multiple Sclerosis Center, 1 Brookline Place, 2nd Floor, Brookline, MA 02445, USA, rbove@partners.org, Tel: 617 525 6550, Fax: 617 525 5333.

The authors declare that there is no conflict of interest.

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Dr. Bove reports no disclosures

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symptoms; and (5) effect of HRT on MS symptoms. Some women reported no effects of menopause or HRT.

CONCLUSION—Given an aging population and a median age of individuals currently living with MS very close to menopausal age in many cohorts, there is a pressing need to understand the impact of menopause on MS course. Qualitative responses in this study illustrated several specific themes that require quantitative testing in clinic-based cohorts.

Keywords

Quality of life; multiple sclerosis; hot flashes; menopause; patient-powered research networks; online communities

1. INTRODUCTION

The onset of multiple sclerosis (MS) is typically during the reproductive years and thus most women will undergo menopause after MS onset. The impact of the long menopausal transition on MS course has only recently been explored. Patient-reported post-menopausal worsening of symptoms was described in 40–54% subjects in two initial small cross-sectional studies but not in a third larger one (reviewed in (Bove et al., 2015)); there was also broad variability in respondents' perceptions of the effect of hormone replacement therapy (HRT) on their MS course. Recently, we found that patient-reported MS severity scores were significantly increased after early menopause and surgical menopause in an analysis of respondents from an online patient-powered platform, PatientsLikeMe.com. (Bove, Healy, 2015)

To begin to close the quantitative research gap regarding the menopausal transition in MS, a relatively new thematic area, qualitative studies (patient interviews, online fora, and focus groups) can provide a complementary approach, by yielding a range of hypotheses that can then be tested in more focused quantitative studies (Lingard et al., 2008). For example, to understand and improve diabetic care, clinical studies (glycated hemoglobin levels, visual examination) can be complemented by qualitative investigations of patients' perceived barriers to glycemic control. The goal of the current case series, a subset of the PatientsLikeMe.com cohort, is to provide such a qualitative approach that highlights specific themes surrounding the effect of menopause on MS course.

2. MATERIALS AND METHODS

2.1. Data Source

PatientsLikeMe (www.patientslikeme.com; PLM) is an online structured research platform, whose members reporting MS are largely comparable in demographic and disease characteristics to a large referral center and a large online patient registry. (Bove et al., 2013)

2.2. Subjects

As previously described, we identified 1,301 female "active users" aged 18 or above from the over 29,750 PLM members reporting MS. We emailed them an invitation to complete an online reproductive questionnaire in June 2012. An automated reminder message was sent

three days later. Members elected to respond (N=513), opt out (N=112), or not respond (N=317); response rate among members who opened their emails was 54%. After 15 days, the survey was closed. (Bove, Healy, 2015)

2.3. Qualitative responses

In addition to previously-reported questions pertaining to reproductive status (age at menarche, pregnancies; use of exogenous hormones; menopausal status) (S Table 1), respondents were also provided with the following general information prior to questions about their menopausal status: “We are interested in learning about how women’s MS symptoms change at menopause. From the literature, there is no clear information on whether symptoms get better, worse, or are unchanged.” At the end of the survey, they were provided with a free form box in which to answer the following question: “We are interested in any comments or questions that you have about the experiences covered in the above questionnaire. Please use the space below for any comments about the survey, your experiences, or information that may help us understand your responses better. If you have no comments at this time, please leave this field blank and hit “Submit Survey” to complete the study.”

We analyzed the free form text responses to generate a set of hypotheses relating to menopausal changes in MS, that could be tested in future quantitative studies. To achieve this, we employed a grounded theory approach (Glaser and Strauss, 1967), which is widely used in qualitative research (Lingard, Albert, 2008)(S Table 2). Specifically, steps of our methodology that are central to the grounded theory approach included: close line-by-line reading by one author (RB) of the qualitative data, identification of “open codes” (concepts anchoring the data), and iterative grouping of these open codes into more “selective” codes. Emerging themes could then be grouped into larger concepts, or categories of menopausal experiences. These larger categories were then ranked by frequency mentioned by individual respondents. Finally, quotes illustrating these individual categories were selected.

2.4. Ethics Statement

Ethical approval for this study was obtained from the Partners Healthcare Human Research Committee Institutional Review Board.

3. RESULTS

3.1. Respondent characteristics

Of the 513 respondents, 212 provided free form text responses, and of these responses, 127 included comments related to menopause or HRT. The remaining responses related to other reproductive factors (effect of menstrual cycles or contraceptives N=28 and of pregnancies N=27 on MS course), to survey factors (e.g. “I had a hard time remembering the dates”; N=16), or to other themes (e.g. “Past emotional stresses and then digestive issues are what led to my MS” N=14). Women providing comments related to menopause had mean (SD) age of 54.3 (7.7); 96% were White (2% Hispanic). Their mean (SD) age at first MS symptoms was 37.8 (12.2), and MS type breakdown was: 57% relapsing remitting, 28% secondary progressive, 12% primary progressive, and 4% progressive relapsing.

3.2. Women's experience of menopause: qualitative responses (Table 2)

The most common thematic categories identified using the grounded theory approach, were (1) perimenopausal onset of MS symptoms, (2) overlap of MS and menopausal symptoms, (3) MS exacerbations and pseudo-exacerbations triggered by hot flashes, and (4) escalation of disease course after menopause, including increasing fatigue and cognitive disturbance. Additionally, several women reported no association between menopause and their MS, typically when MS onset had occurred long before or after menopause. Finally, some women reported improved MS symptoms on HRT. Representative responses are presented in Table 1.

4. DISCUSSION

Many women with MS are approaching menopause, with heretofore unexplored questions about the role of menopause on their MS course, and possible therapeutic implications. In this case series, we sought a descriptive, complementary approach to quantitative assessments.

In the current study, response biases to the free-form field likely included survey fatigue and the fact that only half of women were post-menopausal. Due to these biases, and to the more widely acknowledged limitations of patient-reported data and of patient-powered platforms (e.g. inability to validate respondents' clinical data, response biases, biases from missing data),(Bove, Healy, 2015) we did not aim to provide a detailed quantification of subject responses. Rather, we identified illustrative free-form responses highlighting themes that may guide new study design.

While most women's first MS symptoms begin during the mid-reproductive years, reproductive events such as menarche and the postpartum period appear to trigger relapses. (Bove and Chitnis, 2014) An effect of menopause specifically on the risk of a first MS relapse has not to our knowledge been quantitatively assessed.

At menopause, a number of symptoms worsen, including symptoms that overlap with MS symptoms (e.g. bladder function, cognition, sleep and mood). Additionally, Uhthoff's phenomenon, or transient neurologic worsening as a result of heat, is well-described in MS and in this case series, MS symptoms appeared to be exacerbated by hot flashes. Therefore, it is possible that during the menopausal transition, MS exacerbations are triggered by hormonal fluctuations and particularly vasomotor symptoms, obscuring a clinician's interpretation of MS course itself. Furthermore, stressful life transitions (employment changes, divorce, parental loss, "empty nest syndrome") often occur at this time, further exacerbating or masking neurologic function.

Finally, patient-reported worsening of MS course after menopause (particularly surgical) is consistent with our quantitative observations, and suggests that gonadal steroid deprivation after menopause may be causally linked with neurodegeneration, as has been observed in healthy and in animal models of MS.(Scott et al., 2014) Furthermore, reported effects of HRT are intriguing, but difficult to evaluate in modern observational cohorts, where few women are placed on HRT.

Given an aging population and a median age of individuals currently living with MS very close to menopausal age, there is a pressing need to understand the impact of menopause on MS course, and optimal perimenopausal management of MS women. Here, we were able to supplement prior quantitative results, with open-ended patient responses highlighting several important themes. These findings warrant further investigation of effects of menopause on MS onset, MS course, and of modulatory effects of hormonal therapies, in other community-based and clinic cohorts.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- In a series of 127 women from an online platform, we describe patient-reported associations between menopause and MS.
- Subjects described perimenopausal worsening of MS symptoms, often due to hot flashes, and an overlap between menopausal and MS symptoms.
- These qualitative responses may be used to generate hypotheses testable in clinical cohorts.

Table 1

Subjective reports of MS subjects' menopausal disease courses highlight a range of experiences for which few empirical data exist. All quotes provided verbatim.

Theme	Respondent age (years)
Perimenopausal onset of MS	
"I have never thought about the subject but my MS really flared after meno and that was when I was dx after being so sick for 15 years"	58
"Menopause and MS were pretty much simultaneous."	60
My first MS attack occurred 3 months after my last menstrual period and right around the time I first started having hot flashes."	55
Effect of hot flashes on MS symptoms	
"When my hot flashes started in beg of 2011 everything got drastically worse. That's the worst my symptoms have ever been. I couldn't write or hold a, pen for, several, months."	37
"I confused the two, especially hot flashes"	53
"About the time my menopause seemed to be bothering me (symptoms of severe hot flashes) is when my MS symptoms really started to be intensified."	48
"A leading MS psych Ph.d thought my observation that hot flashes aggravated my MS was ridiculous but I -- 15 yrs later -- maintain they did in terms of strength"	48
Overlap of MS and menopausal symptoms, and life changes	
"Please keep in mind that I was not officially dx'd when I had my complete hysterectomy. I also must mention that I was busy taking care of elderly ill parents constantly and had very little time to donate to myself or to think about my own health issues."	49
"I did not know i had MS. But did have some symptoms such as numbness, vertigo, fatigue, tingling off and on once I started menopause"	53
"I went through 2 surgeries, divorce and diagnoses all at the same time, hard to determine amount of stress, anxiety and depression and MS change."	45
Worsening of MS-related disability after menopause, particularly surgical	
"Before I stopped taking birth control pill's I was working and able to walk and houseclean etc. I had the surgery and I started to progress toward becoming completely wheelchair bound walking only by dragging and swinging my legs with the help of two canes."	53
"Relapsing-remitting MS seemed more unstable; smaller flare-ups that the neurologist often called "decompensation" [….] Examples: numbness or tingling in hands or feet"	54
"My first noticeable relapse was July of 1995, while still menstrating. In September of 2010, after menopause, symptoms and lesions progressed rapidly."	49
Since my hystorectomy my MS symptoms have increased and progress more rapidly Im not sure if it is due to hormone replacement or age or what	60
I didn't have MS until 1 year after my complete hysterectomy I had it at age 29 and developed MS at 30	47
No relationship between MS and menopause (e.g. MS onset much prior to or after menopause)	
"do not believe menapause cause worst symptoms. age and progession of MS more realistic considering have had over 25 years"	50
"Hysterectomy in 1986. MS diagnosis in 2011. Not sure if we can correlate them or not"	58
"I can not tell you changes when periods stopped, because I hadn't been diagnosed with MS way back then"	55
"I have PPMS and was not diagnosed until after menopause & HRT treatment, so many of the questions may not be applicable"	67
"I was not diagnosed with RRMS until AFTER menopause and I know many other women who were also dx'd later in life."	57
Effect of HRT on MS symptoms	
"None that I can tell at this point"	49

Theme	Respondent age (years)
“I truly believe that stopping the hormone therapy caused my MS to be much worse. I always wonder if I had been allowed to stay on the HRT I may not be disabled as much as I am.”	61
“I am still on HRT and am afraid to go off of it even though I am 52 years old. I feel like I would rather risk the side affects of staying on it than take the risk of going off of it and have it mess with my MS.”	52
“My mother had MS. She was much worse after menopause. As for myself mine got worse immediately after surgery. Once I was on estrogen I did pretty well.”	54
“I am not taking any [estradiol] now because the insurance company refuses to pay for a more expensive brand that does help with my hot flashes which at times cause a lot of fatigue due to heat intolerance.”	49
“[HRT was] beneficial as I believe the absence of hot flashes and increased sense of well-being improved my MS symptoms caused by heat and low energy.”	48
“I always felt better during pregnancy and early on with HRT Last trial of HRT no effect”	65
“I don’t think that without HRT it would have been good at all the anxiety, hot flashes, over all horrible issues with menopause at such a young age (29) and at the time I did not realize many issues I was experiencing were MS related - I was not yet diagnosed”	49