Short Communication

Effect of the Women’s Health Initiative Study Publication on Hormone Replacement Therapy Use among Women Who Have Undergone BRCA1/2 Testing

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Abstract

Background: Since the publication, in July 2002, of the Women’s Health Initiative (WHI) study, use of hormone replacement therapy (HRT) has decreased substantially in the general population. However, little is known about the effect of WHI study results on HRT use among women at high risk of breast cancer. The purpose of this study is to compare HRT use, prepublication versus postpublication of the WHI study, among women tested for BRCA1/2 mutations.

Methods: Participants were >35 years of age and had received their result of genetic testing (delivered within the interdisciplinary research program Interdisciplinary Health Research International Team on Breast Cancer Susceptibility), no later than February 28, 2005. HRT use was reported in self-administered questionnaires, 1 year after result disclosure. Women returning their questionnaire before July 17, 2002 were classified as pre-WHI, whereas those returning it after October 15, 2002 comprised the post-WHI group.

Results: Four hundred fifty-seven women (199 and 258 in the pre-WHI and post-WHI groups, respectively) were included in this analysis. Globally, there was no difference in HRT use between prepublication and postpublication of the WHI study (8% and 11%, respectively; prevalence ratio, 0.74; 95% confidence interval, 0.43–1.28). However, noncarriers of the familial mutation were less likely to use HRT after publication of the WHI study results (9%) than before (21%; P = 0.03). Conclusions: Overall, HRT use among women tested for BRCA1/2 mutations is relatively low and apparently uninfluenced by the WHI study findings. However, the HRT use reduction among noncarriers is similar to that of women in the general population and consistent with the Canadian Cancer Society’s recent HRT use recommendations. (Cancer Epidemiol Biomarkers Prev 2007;16(1):157–60)

Introduction

Since the publication, in July 2002, of the first Women’s Health Initiative (WHI) study results associating combined hormone replacement therapy (HRT) with a significant increase in both coronary heart disease and breast cancer among postmenopausal women (1), HRT use has decreased substantially in the general population (2, 3). However, little is known about the effect of WHI study results on HRT use among women whose family history places them at high risk of breast cancer. In a study conducted before publication of the WHI findings, we reported HRT use as being roughly thrice lower among women whose family history places them at increased risk of breast cancer. Thus, documented knowledge of typical reactions of other women confronted with a similar choice may help providers when counseling high-risk women to make an informed decision. The purpose of this study is to compare HRT use, prepublication versus postpublication of WHI study results, among women who underwent genetic testing for breast cancer susceptibility than among women in the general population, which suggests that high-risk women tend to avoid HRT when BRCA1/2 mutations are either suspected or confirmed (4). A more recent study found a greater prevalence of HRT use among BRCA1/2 carriers than noncarriers (5). However, as BRCA1/2 mutation status was determined after assessment of HRT exposure in that study, no conclusion can be drawn about the effect of a known BRCA1/2 test result on HRT use.

Because there are no clear-cut recommendations about HRT use to alleviate menopausal symptoms in women who undergo BRCA1/2 genetic testing, those considering HRT should be counseled about its risks and benefits. A better understanding of HRT use in this population can be useful in the provision of genetic services. The decision to take HRT for relieving menopausal symptoms is a difficult one for a woman at increased risk of breast cancer. Thus, documented knowledge of typical reactions of other women confronted with a similar choice may help providers when counseling high-risk women to make an informed decision. The purpose of this study is to compare HRT use, prepublication versus postpublication of WHI study results, among women who underwent genetic testing for breast cancer susceptibility. We examine whether the WHI study publication is associated with a decrease in HRT use in this population and explore the characteristics associated with HRT use since the WHI study publication.
Materials and Methods

This study is part of the multidisciplinary research program, Interdisciplinary Health Research International Team on Breast Cancer Susceptibility, which provided BRCA1/2 genetic testing to French-Canadian individuals in the province of Quebec (6). In accordance with genetic testing practice standards (7), pretest education and result disclosure sessions were offered to BRCA1/2 test candidates (women >18 years of age with an extensive family history of breast cancer or ovarian cancer, i.e., three first-degree relatives or a combined total of four first- or second-degree relatives with breast or ovarian cancer). The pretest education session was conducted either by a certified genetic counselor or by a nurse specially trained in oncogenetics. Depending on the hospital where the participant was recruited, the result disclosure session was done by a medical geneticist, a medical oncologist, or a family physician with extensive training in oncogenetics and also involved the genetic counselor/nurse. All women tested for BRCA1/2 mutations in this program since August 1998 were invited to participate in a psychosocial study assessing quality of life and health-related behaviors. Participants may have received a conclusive test result as being a carrier or noncarrier of the familial mutation or an inconclusive result when all individuals tested within the family were negative for the analyzed panel of BRCA1/2 mutations reported previously in the French-Canadian population (see refs. 8, 9 for further details on this psychosocial study and the BRCA1/2 analyses carried out in this program). All women aged >35 years of age who had received their test result no later than February 28, 2005 were eligible for these analyses, thus excluding subjects who chose to remain unaware of their test result. The decision to include women aged >35 years was based on the current oophorectomy recommendation not to do this surgery on women under 35 years of age, as they are still in their child-bearing years and have a lower risk of ovarian cancer. This study was approved by the Institutional Ethics Review Boards of participating hospitals and all participants signed informed consent forms.

Information on current HRT use 1 year postdisclosure of BRCA1/2 test result was reported using a self-administered, mail-in questionnaire providing data on age, education, marital status, parity, personal cancer history, and oophorectomy status. Women who returned the 1-year questionnaire before July 17, 2002 were classified as pre-WHI whereas those who returned it 90 days or more after the WHI study publication (i.e., October 15, 2002) comprised the post-WHI group.

Crude and adjusted associations between the WHI study period, participant characteristics, and HRT use were measured by prevalence ratios with 95% confidence intervals using binomial regression models. The potential confounding effect of several variables was assessed by comparing crude and adjusted models. Potential confounder variables were age, education, cancer history, oophorectomy status, and BRCA1/2 test result. Age was used as a proxy for menopausal status (<50 and ≥50 years), which was not assessed in the current study. In each model, the interaction effect of the BRCA1/2 result and WHI period was also assessed. To control for the potential effect of familial clustering, the analyses were repeated using the generalized estimating equation approach (8). However, because the design effect due to familial clustering was low (1.05), it was not taken into account. Sensitivity analyses were done with longer time lapeses (120 and 150 days) between the pre-WHI and post-WHI periods to assess result robustness. Statistical analyses were done using SAS software 9.1 (9).

Results

Between August 1, 1998 and February 28, 2006, of the 570 women who participated in the psychosocial study and received their genetic test result at least 1 year earlier, 18 (3%) refused to participate, 22 (4%) were lost to follow-up, 12 (2%) did not receive a questionnaire, and 5 (1%) provided incomplete information about HRT use. Of the 513 (90%) women for whom HRT information was available, 28 were further excluded from the analyses because their questionnaire was completed between July 17, 2002 and October 15, 2002, which did not correspond to either the pre-WHI or post-WHI periods. Of the remaining 485 women, 28 were excluded as being under 35 years of age 1 year postdisclosure. Thus, analyses are based on 457 women, 199 and 258 in the pre-WHI and post-WHI groups, respectively.

Overall, both groups were similar with respect to age, parity, personal cancer history, and oophorectomy status (Table 1). However, proportionally more women had an inconclusive test result in the post-WHI period than in the pre-WHI period. Post-WHI subjects were generally better educated and more likely to be living with a spouse than the pre-WHI women.

Globally, there was no significant difference in pre-WHI and post-WHI study publication HRT use, 8% and 11%, respectively (prevalence ratio, 0.74; 95% confidence interval, 0.43-1.28; Table 2). HRT use varied according to age group with women 50 to 59 years of age and ≥60 years being roughly three and four times, respectively, more likely to use HRT than women in the 35 to 49 years age group. Women with a history of cancer were less likely to use HRT than unaffected women (prevalence ratio, 0.29; 95% confidence interval, 0.13-0.64). Although the prevalence of HRT use among mutation carriers (3%) tended to be lower than noncarriers (16%), this difference was not significant after adjustment for potential confounders. Only three carriers were using HRT 1 year postdisclosure, two of whom (aged 39 and 43 years) had undergone a prophylactic oophorectomy. The test of interaction between the WHI period and BRCA1/2 test result indicated the difference in HRT use between the pre-WHI and post-WHI periods varied according to test result (P = 0.15). Specifically, noncarriers were less likely to use HRT following publication of the WHI study results (9%) than before (21%; P = 0.03; Fig. 1). HRT use was low among carriers and similar for both periods. Finally, HRT use

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Pre-WHI (n = 199), n (%)</th>
<th>Post-WHI (n = 258), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>35-49</td>
<td>66 (33)</td>
<td>79 (31)</td>
</tr>
<tr>
<td>50-59</td>
<td>69 (35)</td>
<td>101 (39)</td>
</tr>
<tr>
<td>≥60</td>
<td>64 (32)</td>
<td>78 (30)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>54.6 ± 10.5</td>
<td>54.6 ± 9.7</td>
</tr>
<tr>
<td>Education (y)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤12</td>
<td>116 (58)</td>
<td>119 (46)</td>
</tr>
<tr>
<td>&gt;12</td>
<td>83 (42)</td>
<td>139 (54)</td>
</tr>
<tr>
<td>Mean ± SD</td>
<td>13.2 ± 6.4</td>
<td>14.6 ± 8.5</td>
</tr>
<tr>
<td>Living with a spouse</td>
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<tr>
<td>No</td>
<td>60 (31)</td>
<td>55 (23)</td>
</tr>
<tr>
<td>Yes</td>
<td>132 (69)</td>
<td>187 (77)</td>
</tr>
<tr>
<td>Has children</td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>39 (21)</td>
<td>41 (17)</td>
</tr>
<tr>
<td>Yes</td>
<td>151 (79)</td>
<td>202 (83)</td>
</tr>
<tr>
<td>Cancer status</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unaffected</td>
<td>113 (57)</td>
<td>147 (57)</td>
</tr>
<tr>
<td>Affected</td>
<td>86 (43)</td>
<td>111 (43)</td>
</tr>
<tr>
<td>BRCA1/2 test result</td>
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<td></td>
</tr>
<tr>
<td>Noncarriers</td>
<td>61 (31)</td>
<td>55 (21)</td>
</tr>
<tr>
<td>Carriers</td>
<td>51 (25)</td>
<td>38 (15)</td>
</tr>
<tr>
<td>Inconclusive</td>
<td>87 (44)</td>
<td>165 (64)</td>
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<tr>
<td>Had oophorectomy</td>
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<td></td>
</tr>
<tr>
<td>No</td>
<td>149 (80)</td>
<td>197 (81)</td>
</tr>
<tr>
<td>Yes</td>
<td>38 (20)</td>
<td>45 (19)</td>
</tr>
</tbody>
</table>

*Because of missing data, the number of participants does not always tally.
among women with inconclusive results remained stable following the WHI study publication.

Discussion

Globally, HRT use among women at high risk of breast cancer tested for BRCA1/2 mutations remains relatively low and apparently uninfluenced by the WHI study findings. This observation is consistent with the idea that awareness of being at high risk of developing breast cancer and being a BRCA1/2 mutation carrier deters women from using HRT to alleviate menopausal symptoms. The same is true, to a lesser degree, of women with an inconclusive result. However, among noncarriers, HRT use decreased substantially following publication of the WHI study findings, a similar reduction to that observed in the general population (2, 3). Despite a family history, the breast cancer risk of noncarriers is similar to that of women in the general population (10). The reduction in HRT use among noncarriers is consistent with the Canadian Cancer Society’s HRT use recommendations issued in the wake of the WHI study findings, which consider that "due to increased cancer risk, women should avoid combination HRT for any reason other than to relieve severe menopausal symptoms that have not responded to any other treatment” (11).

The observation that oophorectomy was not statistically associated with HRT use and that very few women who had undergone prophylactic oophorectomy were actually using HRT at the time of the study highlights the lack of formal consensus about hormonal management of high-risk women following induction of surgical menopause. Prophylactic oophorectomy is increasingly offered to BRCA1/2 carriers in an effort to lessen their risk of breast and ovarian cancer (12-14). An immediate consequence of this surgery is surgical menopause and related symptoms (15). For high-risk women, making the decision to use HRT for relieving menopausal symptoms is difficult. In light of the growing body of evidence that short-term HRT use does not reduce the protective effect of prophylactic oophorectomy on the risk of breast and ovarian cancer among BRCA1/2 mutation carriers (15), developing new decision-making tools may be valuable for women considering this option.

This study presents potential limitations worthy of consideration. First, information on HRT use was self-reported,
which could have induced a reporting bias leading to either underestimated or overestimated HRT use. However, because we collected information about current HRT use, it is unlikely the women would fail to remember HRT use. Second, the type of HRT, treatment period, and daily dosage were not taken into account. Yet, it is currently recommended that HRT use among carriers be as short a duration as possible and consists of estrogens only (16, 17). Nonetheless, given the already low prevalence of HRT use in this population, it is improbable that stratifying for type, duration, or dosage would have changed our conclusions. Third, the cross-sectional design of this study makes it impossible to assess how many women discontinued (or initiated) HRT following the WHI study publication. Fourth, this study did not assess the information sources women may have drawn upon when deciding whether to use HRT. Some may have received information as part of their genetic testing follow-up, others from a regular appointment with a physician, and others from media coverage of the WHI report. Futures studies are needed to elucidate how health professionals might take advantage of media focus on issues, such as the WHI report. Fifth, although identifying the pre-WHI period was relatively straightforward, determining the post-WHI period cutoff date was less so. In this study, we considered the post-WHI period onset as 90 days following first publication of the WHI study findings. Although this may seem short for a behavioral or lifestyle change, sensitivity analyses carried out for longer time lapses between the WHI publication and HRT assessment did not change any of our conclusions. Finally, our study population was French-Canadian and had relatively stringent inclusion criteria. Certainly, individuals with fewer affected relatives are having genetic counseling and testing and making HRT decisions. As such, the study population may be different from populations seen by most cancer genetic service providers. However, these differences do not suggest that the study population would behave any differently than other populations about HRT use.

Our descriptive findings highlight the need for future theoretically grounded studies to identify mechanisms that may influence health behavior changes in the context of BRCA1/2 testing. With respect to HRT use in particular, relevant factors could include beliefs about personal risk of cancer, beliefs about the effects of HRT, self-efficacy beliefs about preventing cancer, and motivation to reduce cancer risk (18). Several existing theories relevant to cancer prevention behavior, such as the Health Belief Model (19), the Cognitive-Social Health Information Processing Model (18), and Leventhal’s Commonsense Model (20), could be used for such purposes. Within this context, there is specific evidence suggesting that preventive behaviors among BRCA1/2 carriers are influenced by cancer knowledge and risk-related beliefs (21).

Media coverage of the WHI study shows the increasing importance of the mass media as a vehicle to communicate medical information to the public. A key challenge for health professionals is harnessing the power of the mass media to help individuals make informed health-related decisions. Although medical information provided by the media is generally credible, its application varies according to individual profiles. For this reason, the media cannot replace one-on-one counseling with health professionals. Their role remains essential in guiding members of the public to apply mass media information to their individual case and make informed health-related decisions. This is particularly true in the rapidly evolving field of oncogenetics, as our increasing knowledge of the effects of gene-environment interactions on cancer risks makes this a formidable challenge.

Acknowledgments

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References

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