Is There an Association Between Meningioma and Hormone Replacement Therapy?

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ABSTRACT

Purpose
Molecular and clinical observations suggest a role of sex steroid hormones in the occurrence of meningioma. However, there is limited and often conflicting data on the use of hormone replacement therapy (HRT) as a possible risk factor for meningioma. The goal of this study was to investigate whether there is an association between a diagnosis of meningioma and either current or past HRT use in women.

Methods
We retrospectively reviewed records in the Mayo Clinic Jacksonville electronic patient database between 1993 and 2003 to identify women with a diagnosis of either symptomatic or incidentally discovered, clinically silent meningioma. Records were also searched to identify women with a documented history of either current or past HRT use.

Results
Of the 355,318 women, ages 26 to 86, evaluated for any medical issue, 18,037 (5%) were documented as current or past HRT users. A total of 1,390 women with a history of symptomatic or incidentally discovered meningiomas were identified, 156 (11%) of whom were either current or past HRT users. A logistic regression analysis, adjusted for age, demonstrated a positive association between a diagnosis of meningioma and HRT use, with an odds ratio of 2.2 (95% CI, 1.9 to 2.6; \( P < .0001 \)). The frequency of meningioma in women with either current or past HRT use was 865 in 100,000, whereas the frequency of meningioma in women without the history of HRT use was 366 in 100,000.

Conclusion
The study provides evidence of a positive association between HRT use and diagnosis of meningioma, and therefore, HRT use may be a risk factor for meningioma.

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INTRODUCTION

The sex difference in the incidence of meningioma is widely established, with the frequency of meningioma twice as high in women as in men.1 Clinical findings suggest that meningiomas may be influenced by estrogen and progesterone based on the observation of a positive association with breast cancer2 and tumor growth during pregnancy and menstruation.3 Molecular and immunohistochemical studies confirm that meningioma is a hormone-sensitive tumor, with approximately 70% of meningiomas expressing progesterone receptors and approximately 30% expressing estrogen receptors.4,5 Proliferation of human meningioma cell lines after exposure to estrogen and progesterone has also been observed.6

On the basis of these observations, there has been much speculation by patients and physicians that hormone replacement therapy (HRT) may be a risk factor for meningioma. This concern has been further highlighted by recent data from the Women’s Health Initiative trial, which identified increased risk of breast cancer, coronary heart disease, ischemic stroke, and venous thrombosis with prolonged HRT use.7 Several studies have tried to elucidate the risk of meningioma in relation to endogenous and exogenous sex hormones,8-14 but the results have been conflicting, especially with respect to HRT. Therefore, the relationship between the risk of meningioma and the use of hormonal supplementation in women remains unclear. The current study was undertaken to investigate whether an association exists between a diagnosis of meningioma and either current or past HRT use in women.

METHODS

We retrospectively reviewed records in the Mayo Clinic Jacksonville electronic patient database between 1993 and
Of the 355,318 female patients evaluated between 1993 and 2003 for any medical issue at the Mayo Clinic Jacksonville, 18,037 (5%) were documented current or past users of HRT. A total of 1,390 women had a documented lesion consistent with meningioma on magnetic resonance imaging of the brain. A histologic diagnosis was not required, but the lesion on neuroimaging had to be interpreted as consistent with meningioma in the official report by the neuroradiologist. All patients with meningioma (n = 1,390) were confirmed to have a history of either symptomatic meningioma or clinically silent, incidentally discovered meningioma, as confirmed by the official neuroradiology report.

A logistic regression analysis, adjusted for age, was used to investigate evidence for an association between a diagnosis of meningioma and the use of HRT. The frequency of meningioma in women with or without the use of HRT was calculated in raw proportions and per 100,000 women. The study was approved by the Mayo Clinic Institutional Review Board.

Table 1. Frequency of Meningioma in Women With and Without History of HRT Use

<table>
<thead>
<tr>
<th>Age Group</th>
<th>Raw Proportion</th>
<th>HRT</th>
<th>No HRT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of Patients With Meningioma</td>
<td>Total No. of Patients</td>
<td>No. of Women With Meningioma per 100,000</td>
</tr>
<tr>
<td>26-55 years</td>
<td>23</td>
<td>3,460</td>
<td>665</td>
</tr>
<tr>
<td>56-65 years</td>
<td>25</td>
<td>4,770</td>
<td>524</td>
</tr>
<tr>
<td>66-75 years</td>
<td>41</td>
<td>4,644</td>
<td>883</td>
</tr>
<tr>
<td>76 years and older</td>
<td>67</td>
<td>5,010</td>
<td>1,337</td>
</tr>
<tr>
<td>Overall</td>
<td>156</td>
<td>18,037</td>
<td>865</td>
</tr>
</tbody>
</table>

Abbreviation: HRT, hormone replacement therapy.

RESULTS

The patients were defined as having a diagnosis of meningioma if they had a documented lesion consistent with meningioma on magnetic resonance imaging of the brain. A histologic diagnosis was not required, but the lesion on neuroimaging had to be interpreted as consistent with meningioma in the official report by the neuroradiologist. All patients with meningioma (n = 1,390) were confirmed to have a history of either symptomatic meningioma or clinically silent, incidentally discovered meningioma, as confirmed by the official neuroradiology report.

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Meningiomas account for approximately 25% of primary intracranial tumors in the United States and are twice as common in women as in men. In vitro studies suggest that meningioma is a hormone-sensitive tumor that often contains both progesterone and estrogen receptors. This finding plus the observation that meningioma cell lines proliferate after exposure to progesterone and estrogen provide molecular and physiologic evidence for a potential role of sex steroid hormones in the development and growth of meningioma.

Clinical evidence suggesting that meningioma might be a hormone-sensitive tumor is based on observations of higher incidence in women than in men, an observed increased growth of meningioma during pregnancy and menses, increased incidence of meningioma in women with breast cancer, and a higher prevalence in women with lymphangioleiomyomatosis, a cystic lung disease that is commonly treated long term with progesterone and other hormonal agents.16

DISCUSSION

Fig 1. Estimated odds ratios and associated 95% CIs for association between hormone replacement therapy use and diagnosis of meningioma.

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In this retrospective study, we found a positive association between a diagnosis of meningioma and HRT use (OR = 2.2; 95% CI, 1.9 to 2.6; P < .0001). The prevalence of meningioma in women with either current or past HRT use was 865 in 100,000, whereas the prevalence of meningioma in women without a history of HRT use was 366 in 100,000.

To our knowledge, this is the largest sample size study that assesses the relationship of exogenous hormone use and meningioma. Two prior studies also found a positive association between HRT and meningioma.16,11 In the Nurses’ Health Study, the relative risk of meningioma was found to be 1.01 (95% CI, 0.49 to 2.1; P = .98) in postmenopausal women who were past users of HRT and 1.86 (95% CI, 1.07 to 3.24; P = .03) in current HRT users.19 Of the 125 women with meningioma in the Nurses’ Health Study, which relied on mailed questionnaires, only 11 women identified themselves as past HRT users, whereas 33 women responded as current HRT users. More recently, Wigertz et al11 examined 178 women with meningioma, 68 of whom responded in interviews as ever using HRT. This study found an increased relative risk of meningioma in postmenopausal women with a history of ever using HRT, with an OR of 1.7 (95% CI, 1.0 to 2.8). Several other studies have attempted to assess the relationship between HRT use and meningioma, but the results were either inconclusive as a result of low statistical power or showed a nonsignificant protective effect of HRT use on meningioma.12–14

When the association between meningioma and HRT use was analyzed according to the age groups, we found that the estimated OR consistently approximated 2 for women older than 56 years. However, for women ages 26 to 55 years, the association was stronger, with an estimated OR of 4.1. This raises the provocative possibility that, in younger women, there may be a stronger effect of HRT on the occurrence of meningioma. We were unable to extract enough information in this retrospective analysis regarding pre- or postmenopausal status or the timing of the first HRT exposure to draw conclusions about a possible relationship.

As expected, we found that the total prevalence of meningiomas in female patients at our institution increased with age, with the highest prevalence (677 in 100,000) being in women age 76 years and older. This finding is consistent with previous reports, which showed an increase in prevalence of meningioma with age.17,18

Our study has several limitations that need to be considered. We recognize the limitations inherent to a retrospective chart review, including a possibility that some women who were current or past HRT users were not documented as such in the medical records. Additionally, there may be a more accurate historical documentation of HRT exposure in women with meningioma compared with women evaluated for other medical issues. Self-reporting of oral contraceptives has been validated in other studies,9,25 but self-reporting of HRT use has not been previously validated.

A number of important questions were raised by our study regarding the impact of HRT exposure, including the type, dosage, duration, and timing, on the development and growth rate of meningioma. These data could not be extracted from the medical chart documentation because they were not often detailed and would be best obtained in the context of a prospective analysis.

Finally, in this study, we did not separate symptomatic meningiomas from those that are clinically silent and discovered incidentally via neuroimaging. As such, it is impossible to determine at this time whether HRT use is associated with symptomatic or radiographic progression of clinically silent meningiomas.

In summary, this is the largest sample size study providing evidence of a positive association between HRT use and a diagnosis of symptomatic or incidentally discovered, clinically silent meningioma. Our findings suggest that HRT use may be a risk factor for meningioma, and future confirmation of these results is needed in the context of prospective studies. Until then, however, clinicians and patients alike should be aware of these data when considering the risks and benefits of HRT.

REFERENCES


