Long-Term Care Updates

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Hormone replacement therapy: Prevention of age-related macular degeneration?

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Introduction

Age-related macular degeneration (AMD) is the leading cause of vision loss in those over the age of 50 years worldwide.[1] By 2050, it is projected that the prevalence of AMD in the United States will increase to 22 million, and globally by 2040 the prevalence is expected to increase to about 288 million. The main risk factors include increasing age, ethnicity, and family history. The American Academy of Ophthalmology (AAO) recommends antivascular endothelial growth factor (anti-VEGF) antibodies as first line treatments (Good Quality, Strong Recommendation). Additionally, AAO provides a discretionary recommendation for the use of vitamin therapies (i.e., zinc, vitamin C, and vitamin E) for intermediate or advanced AMD.[2]

While there is interest in using hormone replacement therapy (HRT) for the prevention of AMD, this approach has yet to be addressed in clinical practice guidelines. The following article will review available evidence on postmenopausal HRT for the prevention of AMD.

Clinical Evidence

A 2021 nationwide retrospective cohort study conducted in Korea evaluated the association between female reproductive factors and the risk of AMD. A total of 1,297,388 postmenopausal patients ≥ 50 years of age were followed for a mean duration of 7.27 years. A self-administered questionnaire was used to collect clinical data on female reproductive factors such as menopause, history of HRT use, and oral contraceptive pill (OCP) use. The study participants had a mean age of around 62 years, 15.5% had received HRT, and 15.2% had previously used OCP. Overall, 4086 participants were diagnosed and treated for AMD during the follow-up period. The use of HRT for ≥5 years (HR 1.72; 95% CI 1.48-2.0) or for 2 to <5 years (HR 1.29; 95% CI 1.09-1.52) was associated with a significantly greater risk of developing AMD when compared to those without HRT use. The researchers found that

a longer lifetime exposure to endogenous and exogenous estrogen was associated with an increased risk of developing AMD. A major limitation of this study was that the data were based on self-reported histories, so the age of HRT initiation, composition/concentration of HRT, and HRT history were not included.[3]

A 2020 case-control study conducted in Colorado set out to determine if the use of menopausal HRT was associated with the development of three forms of AMD (neovascular (NV), geographic atrophy (GA), and early/intermediate). A total of 541 participants, with 409 having a diagnosis of AMD (n=186 for NV; n=61 for GA; n=162 early/intermediate) and 132 serving as controls were included. The historic and current use of HRT was assessed via interview and verified by a review of the patient's medical record when available. However, information regarding the type of therapy (i.e., estrogen or progestin), dosage, duration, and dosage form was not collected. The researchers found that any use of HRT was found to be significantly protective for each type of AMD with early/intermediate AMD (OR 0.36 95%CI: 0.22-0.61), GA (OR 0.40 95%CI: 0.20-0.80), and NV (0.31 95%CI: 0.18-0.54), supporting the fact that a protective relationship between the use of HRT and AMD have been previously identified in literature. One major limitation of the study was that the use of HRT itself may actually be a confounder because other exogenous estrogen exposures (i.e., use of oral contraceptives, age of menopause) could play a role in the development of AMD or increase the likelihood of HRT use.[4]

A 2008 cohort study investigated whether exposure to estrogen was associated with a lower risk of developing AMD. A total of 970 cases of AMD in postmenopausal subjects were included in the analyses. Participants were administered questionnaires that asked for the brand name and/or type and total duration of use of each HRT medication. Current HRT users experienced a 34% higher risk of early AMD (RR 1.34; 95%CI: 1.06-1.68) but a 48% lower risk for neovascular AMD (RR 0.52 95%CI: 0.38-0.71). Additionally, there was no observed benefit for those who have never used HRT during menopausal years.[5]

The 2006 Women's Health Initiative Sight Exam study examined the effectiveness of conjugated equine estrogens (CEE) or CEE combined with progestin (CEE+P) in 4262 females ≥65 years old for the prevention of AMD. A total of 2635 participants were assigned to receive CEE 0.625 mg/d + progestin 2.5 mg/d and 1627 received CEE 0.625mg/d, respectively. The primary outcome was any type of AMD (no AMD, minimal early AMD, moderate early AMD, severe early AMD, and 2 stages of late AMD). The overall prevalence of any form of AMD was 21%. The authors did not identify any association between the use of CEE +P (OR 0.91 95%CI: 0.75-1.11) or CEE (OR 0.98 95%CI: 0.78-1.25) and early-stage AMD. However, they did observe a reduced risk of neovascular AMD with the use of CEE+P (OR 0.29 95%CI: 0.09-0.92). The researchers concluded that treatment with HRT alone does not prevent the occurrence of early AMD but that it may offer a possible protective effect for neovascular AMD.[6]

The 2005 Salisbury Eye Evaluation Project was a cross-sectional study that evaluated 1458 patients between the age of 65 to 84 living in Salisbury, MD in 1993. Participants were administered questionnaires that collected data about HRT use (including information about dose, duration, and time since use), reproductive history, and medical history. A total of 460 females reported current or past HRT use, and about 10% reported taking HRT at the time of the study. The authors did not find any statistically significant correlations between HRT use and early (OR=0.7) or advanced forms (OR=0.6) of AMD, but the odds ratio was <1 for AMD. A major limitation of this study was that power was too low to detect an association between current HRT use and advanced AMD.[7]

Conclusion

Currently, published research is of low-quality, lacks key detailed data, and presents mixed results on the use of postmenopausal HRT for the prevention of AMD. Further high-quality studies are needed to establish whether HRT has a significant impact on the prevention of AMD in older adults.

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