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Post-Reproductive Health. Opportunity Window For The Prevention Of Co-Morbidities

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Abstract

Menopausal hormone therapy (THM) is fraught with controversy, and post-reproductive health is quite challenging. It has gone through many years of ups and downs. We recognize that comorbidity is more common after menopause, and we must need preventive measures to avoid it. When THM was used uniformly, the risk-benefit ratio became unfavorable, and its usage plummeted; nevertheless, more recent studies also introduced the idea of a "window of opportunity," in which THM has no negative side effects and actually prevents comorbidities associated with menopause.

Keywords: Menopause, HRT, MHT Window of Opportunity, Post-Reproductive Health

BACKGROUND

Millions of women around the world face health problems after menopause, and a large proportion of them have a longer life span at birth, despite the fact that the average age of menopause is only 46 years. Maintaining positive post-reproductive health, preventing illness, lowering mortality rates, and improving quality of life are all important goals. Menopausal hormone therapy (MHT) has been linked to a number of advantages, but it is also linked to a number of complications, including breast cancer and thromboembolism, which exacerbates the already elevated risks associated with morbidity, age, and pregnancy. menopause is a term used to describe a period of time MHT is a window of opportunity to reduce the related risks of comorbidities after menopause in the prevention of comorbidities 1-5.

Cardiovascular diseases are the leading cause of morbidity and mortality worldwide; the risk of cardiovascular diseases rises with age in both men and women; however, in women, the risk is delayed until menopause due to estrogen's cardioprotective impact. Other major morbidities include osteoporosis-related fractures and cancer. Cerebrovascular accidents, pulmonary embolism, dementia, breast cancer, and endometrial cancer (can occur as a side effect of MHT, Table 1; The highest occurrence of heart disease in women occurs after menopause, oestrogen/progesterone MHT was administered to menopausal women to minimize the risk of heart disease prior to the findings of the Women's Health Initiative report (WHI)6.

Table 1

Morbidities related to age, menopause and MHT

- Cardiovascular morbidities
- Deep venous and pulmonary embolism
- Dyslipidemia
- Diabetes

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- Dementia
- Breast cancer
- Endometrial cancer
- Ovarian cancer
- Cervical cancer

Osteoporosis-related fractures

THM is not recommended for primary or secondary prevention of coronary heart disease, according to the Women's Health Initiative (WHI) with Heart and Estrogen and Progestin Replacement (HERS) 6 report, which reduced its widespread use after menopause. Although the WHI study was terminated after seven years, 27,347 postmenopausal women aged 50 to 79 were tracked for a total of 13 years without receiving any care.

Despite the fact that postmenopausal women are more aware of MHT-related problems, they now seek treatment only if they have symptoms, with some hoping to stay young forever and improve their quality of life. Since universal MHT use is no longer recommended, how do we choose which women to treat with MHT in order to monitor symptoms, avoid comorbidities, and improve their quality of life? What tactics do we use to achieve the best possible combination of THM's risks and benefits? Although the answers to these questions are unclear, the newly adopted "window of opportunity" principle can be useful in achieving the goals.

The "time hypothesis" or "window of opportunity" for starting the THM suggests that MHT should be provided soon after menopause for a short period of time. MHT that begins several years after menopause and continues for a long time has been linked to further side effects; however, WHI data showed that MHT was not linked to significant complications in women aged 50 to 596.

Other studies (7-9) also sparked interest in MHT as a result of promising findings with a beneficial impact on coronary artery disease; hormone therapy initiated soon after menopause (up to 7 months postmenopause) substantially decreases coronary artery disease mortality.

It also showed a lower occurrence of heart failure and myocardial infarction in women under the age of 50 in the first three years after menopause, without raising the risk of thromboembolic events, stroke, or cancer. The calcium score in the coronary artery was used to assess the development of carotid artery intima-media thickness and atherosclerosis; there was no evidence of a rise in carotid intima-media thickness or a higher incidence of atherosclerosis, supporting the idea of the window of opportunity, which is when starting MHT in early postmenopause has a net gain 9. Only when MHT is used during this "window of opportunity" era does it reduce the risk of cardiovascular disease. As a result, the best option for lowering the risk of coronary heart disease and general mortality in women will be to begin hormone therapy within 10 years of menopause and/or before 60 years of age, for a limited time. MHT is risky after 60 years of age because the vascular lumen is partly obliterated with atherosclerotic plaques due to advanced age; MHT can render the plaque unstable, decreasing vasodilation, and thereby increasing the risk of cardiovascular disease. 10; The results of using THM 11 for the primary or secondary prevention of CVD or for the protection of cognitive function were not indicated; however, it should be noted that only 30% of the women in the study were 50 to 59 years old at the start; the occurrence of venous thromboembolism increased, although no other risk was observed. MHT may help slow the progression of atherosclerosis if started early before it becomes developed.

Endogenous Estrogen and Comorbidities

Endogenous estrogen has a number of positive and protective effects, including slowing the onset of age-related diseases. Menopause brings with it an increased risk of vasomotor symptoms (VMS), osteoporosis, cardiovascular disease, cancer, and dementia due to hypoestrogenism. Estrogen protects against atherosclerosis, inflammatory changes, and lipids with high and low-density lipoproteins (HDL and LDL), preventing cardiovascular events. Estrogen causes vasodilation and reduces cardiovascular risks by acting on endothelial vessels and smooth muscles.

Biomarkers of Vasomotor Symptoms of Cardiovascular Diseases and the Window of Opportunity

SVMs can be used as biomarkers for cardiovascular disease, according to evidence 12. THM has been shown to be effective in reducing SVMs associated with menopause in women of all ages. If MHT is initiated for symptomatic women before the age of 60 or within 10 years after menopause, comorbidities may be avoided. Non-hormonal alternatives should only be used if MHT is contraindicated or if the patient refuses it. SVMs could be used as a biomarker for cardiovascular diseases, assisting in the identification of patients that would be on THM for the longest time5,6.

THM on vasomotor symptoms, mood swings and osteoporosis

According to the most recent data, all women with SVM are likely to have a lower bone mineral density (BMD); women aged 50-79 years with moderate/severe SVM had lower BMD in the femoral neck and lumbar spine, as well as higher rates of hip fractures over an 8-year follow-up period than women without SVM 13. MHT reduces the risk of fractures by focusing on these symptomatic women for the prevention of osteoporosis-related morbidity and mortality. MHT may be initiated in postmenopausal women at risk of fracture or osteoporosis during the window of opportunity, however beginning after 60 years necessitates a unique method. 1-6.

THM supports early postmenopausal women with mood swings. THM can also be beneficial for women going through menopause (TM) who are depressed. Some women with suicidal impulses benefit from MHT, but in this case, antidepressant therapy should be considered first in consultation with a psychiatrist. 6.

Reduction of comorbidities related to the administration, routes and duration of MHT

When started in women younger than 60 years and/or within 10 years of menopause, there is a wide body of high-quality evidence indicating that estrogen-only MHT reduces the incidence of myocardial infarction and also mortality from other causes. When the uterus is intact, however, estrogen-only therapy is not prescribed, so progesterone must be added to prevent the development of endometrial cancer (EC).

In comparison to the estrogen-alone community, evidence on estrogen plus progestogen therapy initiated in women younger than 60 years or within 10 years of menopause shows mixed results. The use of lipid-friendly molecules such as natural progesterone and dydrogesterone may be favoured to minimize progesterone-related morbidity; however, oral THM has not been shown to reduce the risk of arterial and venous thromboembolism (VTE).

The use of medroxyprogesterone is linked to an increased risk of breast cancer (MC). MHT taken in the early stages of menopause has been shown to reduce the risk of Alzheimer's disease later in life 14. The use of oral MHT in older women has been linked to an increased risk of dementia.

MHT should be used in low doses for the shortest possible time before the age of 60 or within 10 years of menopause, according to the world consensus; women with VMS after the age of 60 may need THM; if it is required after the age of 60, an individual risk calculation must be done to keep morbidities to a minimum. VMS is short-lived and vanishes within two years, according to a recent report. Since VMS may last for years, they may not be properly included in the "short-term symptoms" of menopause.

The VMS lasted for more than 7 years, with more than half of the women experiencing symptoms for 4.5 years after their last menstrual cycle 15. MSV was found in 39.2 percent of women aged 65 to 79 years, while VMS was found in the highest percentage of women aged 65 to 69 years 16 and it is not advised to stop taking systemic estrogen at the age of 65. The dosage, type, and route of administration of MHT should be chosen based on the treatment goals, patient preferences, and risk factors; therefore, it must be personalized.1-6.

On an annual basis, the risk profile must be re-evaluated. Some women can need it for a longer period of time. After consulting with the patient, a decision should be taken about how to begin MHT and when to stop it. Supervision of specialists is needed for this. Hormone treatment can be dangerous for women who already have heart disease, cerebrovascular disease, or thromboembolic tendencies. If THM is indicated in the presence of high-risk factors, transdermal preparations are favored. Non-hormonal medications are available for the treatment of SVM associated with TM and early menopause, and women should be aware of them. Premature menopause necessitates the use of a regular THM dosage before the age of normal menopause, after which it should be stopped with caution.

DISCUSSION

MHT is used to treat menopausal symptoms and maintain BMD 1-5,17, and it has been shown to lower cardiovascular risk, particularly when started soon after menopause 18. To women with a uterus 17, estrogen is needed with the addition of a progestogen. While progestogens in THM regimens are linked to about one case of breast cancer per 1000 women per year among current THM users, micronized progesterone or dydrogesterone 19 may be linked to a lower risk 20,21.

When it comes to the risk of VTE, the form of progestogen matters, with micronized progesterone and dydrogesterone appearing to have the lowest risk 22. Progestogens have no effect on estrogen-induced reductions in total and LDL cholesterol 23,24, but CEE and CEE / MPA regimens have beneficial effects on lipids. Estradiol's potentially beneficial effects on insulin tend to be unaffected by dydrogesterone. 25.

Individual risk factors, patient preference, and clinical environment must all be considered since there is no existing guideline on the option of progestogen for use in HRT in the UK 26-28.

CONCLUSION

The window of opportunity or time hypothesis has cardiovascular benefits when MHT is initiated immediately after menopause; THM should not be used regularly for the primary or secondary prevention of CVD. Further research into the function of natural progesterone versus synthetic progestins is required. In order to minimize cardiovascular risk in menopausal women, healthy lifestyles and alternative interventions should be promoted. THM is a medication that increases one's quality of life. After adequate counseling and a comprehensive risk-benefit discussion, the initiation, path, and length of MHT should be customized for each patient. The secret to providing the best combination of risks and benefits to avoid both menopause and MHT-related comorbidities is to start MHT early in women who are chosen during the window of opportunity.

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