Early in 2007, there were 2 regional scientific meetings in menopause, i.e. the 3rd Scientific Meeting of the Asia Pacific Menopause Federation (APMF) and Menopause Academic Conference (MAC) 2007. The APMF was established in 1999. The council of the federation included the representative menopause societies from 14 neighboring countries in the Asia-Pacific region. The APMF planned to conduct a 3-yearly regional scientific meeting. The 3rd APMF meeting was held in Taipei, Taiwan, from March 1st to 4th, 2007, under the theme of ”From Basic Science to Clinical Practice on Menopause”. The Menopause Academic Conference (MAC) is a Thai conference in menopause medicine conducted under the collaboration of 5 institutes with expertise in menopause medicine. MAC is actually the replacement of annual scientific meeting of the Thai Menopause Society (TMS) which was established in 1993. The 3rd MAC was held in Bangkok, from March 21st to 23rd, 2007 under the theme of ”Cutting Edge in Menopause Medicine”.

Various topics were discussed in these 2 meetings. One interesting topic is postmenopausal hormone therapy (PHT) which has had major changes during the past decade.

**Hormone and Cardiovascular Disease**

Before 1998, all postmenopausal women were recommended to consider PHT for the prevention of cardiovascular disease (CVD) and other degenerative diseases. In 1998, the result of a large randomized controlled trial (RCT), the Heart and Estrogen/progestin Replacement Study (HERS), was published. HERS showed that a standard regimen of PHT (0.625 mg of conjugated equine estrogen plus 2.5 mg of medroxyprogesterone acetate, CEE + MPA) has no benefit for secondary prevention of CVD. In 2002, the first data of the ever largest RCT on PHT, Women’s Health Initiative (WHI) study, was released, aggravating bad news on PHT. It showed that the standard dose of PHT has no benefit for primary prevention of CVD, either. These 2 RCTs were a Tsunami and its after-shock for PHT. As a result, the recommendation for PHT was dramatically changed. PHT is recommended only for symptomatic women, not for the prevention of chronic disease, and at ”the lowest effective dosage” for ”the shortest duration” as necessary.

Shortly after, re-analysis and subgroup analysis of the WHI study and a previous large cohort study, the Nurses Health Study (NHS) showed that PHT is beneficial for the women who started to use PHT in the early postmenopausal period, i.e. younger than 60 years of age or less than 10 years post menopause. The results raised the ”Window of Opportunity” concept which suggests that the appropriate timing of PHT initiation (i.e. around or shortly after menopause) would be beneficial for cardio- and probably neuro-protection. Commencement of PHT later from this period gives no benefit or even adverse effects on CVD. Data from in vitro and animal studies support this concept. As blood vessels retain estrogen receptors for only a few years after menopause, it gives a therapeutic window of opportunity of PHT on the blood vessels, which are very important for the function of cardiovascular and nervous systems.

**Hormone and Cognition**

Functions of nervous system decline with age. Observational studies suggested that PHT could delay cognitive impairment in postmenopausal women. However, data from the WHI study did not support the finding from observational studies. The WHI study showed that PHT prescribed in late postmenopausal women, i.e. older than 65 years of age, has no benefit and may have adverse effects on cognitive function, probably due to the increase in vascular dementia. Nevertheless, recent data from an observational study suggested that the initiation of PHT during the window of opportunity period may be able to preserve cognitive function in postmenopausal women.

**Low Dose Hormone Therapy**

Data from the WHI study confirmed that a standard dose PHT has side-effects including breast cancer, venous thrombo-embolism, CVD, and stroke. Many assumptions were used to explain the causes of such side effects. Various strategies to reduce the side effects have been investigated. One of those strategies is the use of lower dose PHT. A large RCT on low dose PHT, the Women’s Health, Osteoporosis, Progestin, Estrogen (Women’s HOPE) study, demonstrated that lower dose CEE with or without MPA is effective in reducing hot flushes and bone loss and improving quality of life. Though the lower dose is not as effective as the standard dose, it is more tolerable as it causes less nuisance side effects including vaginal bleeding and breast tenderness. Previous observational studies demonstrated that risks of serious side effects, i.e. DVT, cardiovascular events, and stroke, increase with higher dose PHT.
Hormones and Breast Cancer

It is now accepted that breast cancer risk increases with the duration of postmenopausal hormone therapy (PHT). Information from many observational studies and meta-analysis showed that all regimens of PHT increases breast cancer risk. Information from an RCT, the WHI study, was slightly different in that only the progestin-containing HT increases the risk. However, the information that estrogen-only HT does not increase the risk needs further confirmation. A report from a large cohort study in France teachers (E3N study) showed that different types of progestin in PHT might have different breast cancer risk. It was possible that the PHT containing natural progesterone or dydrogesterone might not increase the risk as compared with the regimens containing other progestins.

CONCLUSION

Current trends in postmenopausal hormone therapy is to start the PHT early in menopause and continue long-term to have a cardiovascular protective effect (the window of opportunity concept). Different dosage, route of application, and types of progestin cause different side effects. However more data on the serious side effects are needed before making recommendation on these conditions. It is still recommended that PHT is prescribed in the lowest effective dose and only for the case with indications.

REFERENCES


Manee Rattanachaiyanont, M.D.