Deutsche Menopause Gesellschaft e.V.

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HOW HEALTHY OR DANGEROUS IS HRT AFTER AGE 65?

Schweizerische Gesellschaft für Gynäkologische Endokrinologie, Kontrazeption und Menopause

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Use of menopausal hormone therapy beyond age 65 years and its effects on women's health outcomes by types, routes, and doses.

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BACKGROUND

In its 2022 position paper, the North American Menopause Society (NAMS, now The Menopause Society, TMS) notes that initiation of hormone replacement therapy (HRT) in women older than 60 years or more than 10 years postmenopausal carries complex risks and requires careful consideration. For women who started HRT within 10 years of the menopause, there is no general rule that HRT should be stopped after the age of 65. HRT can be continued, for example if hot flushes persist, after an individual assessment of the benefits and harms [1]. However, many doctors are reluctant to prescribe HRT for women over the age of 60, particularly because of the fear of cardiovascular events.

SUMMARY OF RESULTS

The aim of this trial was to assess the health effects of HRT in women aged 65 and over. The outcomes were all-cause mortality, malignancies (breast, ovarian, colorectal, lung, endometrial), cardiovascular disease (myocardial infarction (MI), venous thromboembolism (VTE), heart failure, stroke, atrial flutter, coronary heart disease (CHD)), and dementia, as in the Women's Health Initiative. The researchers analysed prescription data from 2007 to 2020 for more than 19 million US women aged 65 and over who were enrolled in Medicare, the government health insurance programme. Medicare covers three groups of patients in the US: people over 65, certain younger people with disabilities and people with end-stage renal disease. Medicare has three components that cover different services: Medicare Part A (hospital insurance), Medicare Part B (medical insurance, including some outpatient care) and Medicare Part D (prescription drug coverage). Different types of estrogen (estradiol (E2), ethinylestradiol (EE), conjugated equine estrogens (CEE)), types of progestogen (bioidentical, synthetic), routes of administration (oral, transdermal, vaginal, injection), dosages (high, standard, low) and combination forms (E2 mono, E2 + progesterone, E2 + synthetic progestogen) were analysed, low) and combination forms (E2 mono, E2 + progesterone, E2 + synthetic progestogen, CEE mono, CEE + progesterone, CEE + synthetic progestogen, EE + synthetic progestogen, progesterone mono, synthetic progestogen mono).The indication for HRT had to be menopausal; indications such as contraception and bleeding disorders were excluded.A woman was defined as an HRT user if she had received at least one prescription.The death cohort included 10,944,328 women with at least 6 months of follow-up, 14% of whom had ever used any form of HRT.The prevalence of comorbidities at baseline was high in both groups and in the HRT group as follows (selection):CHD 27.3%, diabetes 23.7%, chronic kidney disease 24.2%, depression 39.9%, anxiety 36.2%, osteoporosis 28.7%, hypertension 67.6%, obesity 27.5%. Some also had 'major events' in their medical history (selection):Deep vein thrombosis 7.1%, myocardial infarction 2.0%, stroke 7.7%, dementia 6.2%, breast cancer 6.6%, colon cancer 1.5%, endometrial cancer 1.4%, ovarian cancer 1.0%.During the 14-year follow-up period (2007-2020), the proportion of women over 65 using HRT halved.Surprisingly, very few women received combined HRT (2007: 1.4% and 2020: 0.2%), even though the proportion of hysterectomised women was only 22.6%.The results show that at age 65 years, estrogen monotherapy was associated with significant risk reductions for all-cause mortality (19%), breast cancer (16%), lung cancer (13%), colorectal cancer (12%), heart failure (5%), venous thromboembolism (3%), atrial fibrillation (4%), acute myocardial infarction (11%), and dementia (2%). For combined oestrogen and progestogen therapy, both oestrogen + synthetic progestogen and oestrogen + progesterone were associated with a 10-19% increased risk of breast cancer.

Oestrogen + gestagen also showed significant risk reductions for endometrial cancer (45%), ovarian cancer (21%), CHD (5%), heart failure (5%) and VTE (5%), whereas oestrogen + progesterone only showed a risk reduction for heart failure (4%).The results suggest that the effects of HRT in women over 65 vary according to the type, route and dose.In general, risk reductions appear to be greater with low doses, vaginal or transdermal administration, and E2 compared with CEE.The study shows that women over 65 who have persistent menopausal symptoms should consider continuing HRT with appropriate counselling and regular risk-benefit assessment.

COMMENT

The study is characterised by its large number of cases and a 'fairly pre-diseased' population, the majority of whom appear to benefit from HRT.However, it also reveals some deficiencies in medical care (only in the USA?!), such as 1) many women received HRT despite absolute contraindication, 2) many women received estrogen mono despite having a uterus, 3) apparently some women still received combined hormonal contraceptives despite their advanced age.It is not clear from the study whether the women had already been taking HRT before joining Medicare and were just continuing, or whether they were new users over the age of 65.The duration of HRT use is also unclear. Vaginal estrogen therapy is reported to be particularly safe, but it remains unclear, at least for us Europeans, whether this refers to local estrogen therapy for the treatment of vaginal atrophy or the systemically active vaginal estrogen therapy (Femring®) available in the USA. Finally, it may be possible to infer from the study that HRT appears to be safer than previously thought after the age of 65.However, it is difficult to make specific recommendations, especially for combined HRT, because of the many unanswered questions.

REFERENCES

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