THE DEBATE ON HORMONE REPLACEMENT THERAPY IN POSTMENOPAUSAL WOMEN

Mamurova Sevara Rovshanovna, Tokhirova Sevinch Shukhratjon kizi

Scientific advisor: Berdiyeva Dilnavoz., PhD., Associate Professor.

Central Asian University, Tashkent, 111221, Uzbekistan

mamurova.sevara@gmail.com https://orcid.org/0009-0003-5507-0225
sevilyataxirova@gmail.com https://orcid.org/0009-0000-2410-8591

Relevance of the study: Menopause is biological aging stage of female organism characterized by the absence of a menstrual period for 12 consecutive months without another identifiable cause. It is a transition that typically occurs between 45 and 55 years of age, with a global average age of approximately 51 years**.** Although menopause is a physiological ovarian aging, it is frequently accompanied by a broad spectrum of symptoms that may substantially impair overall well-being. They vary by system or functional domain (cardiovascular, genitourinary, gastrointestinal, psychological, skeletal and breast- related) involved, as well as their severity. According to clinical investigation found approximately 45.8 % of total studied population having moderate symptoms and 52.7 % having severe symptoms. Given the high prevalence and clinical burden of moderate to severe symptoms, therapeutic intervention is often required. These symptoms are primarily managed with hormonal replacement therapies. However, correlation with long-term health risks involving cardiovascular, genitourinary, hepatobiliary system pathologies, as well as uterine and breast neoplasms is present.
Considering the global demographic context, the public health relevance of menopause becomes even more apparent. It is estimated that around 45 million women globally reach the age of 51 each year, which is equivalent to the combined population of Uzbekistan and Netherlands. This illustrates the massive scale of the population who are affected not only by the clinical manifestations of the physiological menopausal transition, but also by medical interventions originally initiated to mitigate symptom severity.

Objective: The objective of this study is to critically evaluate the benefits and risks of hormone replacement therapy, with particular emphasis on dose-duration-dependent effects, current clinical guidelines, and individualized risk–benefit assessment, while exploring future directions for optimizing therapeutic strategies in menopausal management. This research aims to contribute to improved clinical decision-making, evidence-based treatment strategies, and enhanced quality of life for aging women. Recognizing menopause not merely as an inevitable stage of aging but as a significant medical and public health concern underscores the necessity of continued research, education, and individualized patient care.

Materials and Methods: A comprehensive review of several systematic reviews, meta-analyses, and primary studies was conducted to evaluate clinical outcomes, adverse effects, complications, and benefits of HRT for menopause.
Results and discussion: Large Randomized Controlled Trials, including the Women's Health Initiative, which included 38,900 women, showed combined therapy increasing breast cancer,

stroke (R=1.21), venous thromboembolism, and coronary heart disease, while reducing fractures and colorectal cancer, while estrogen-only elevates risks of stroke (RR=1.27) and venous thromboembolism without increasing breast cancer. Bone outcomes were dose- and duration-dependence with higher estradiol doses and longer therapy increasing lumbar spine bone mass density by 14.5%. Meta-analyses confirmed considerable fracture reductions by 34% of vertebral fractures and 29% of hip fractures. Overall, hormonal replacement therapy efficacy and safety depend on type, dose, duration, and patient selection.
The findings indicate that hormonal replacement therapy remains the most effective therapy for moderate to severe menopausal symptoms and for prevention of osteoporosis-related fractures. Nevertheless, its risk profile varies substantially depending on patient age, timing of initiation, dosage, and treatment duration. Moreover, bone protection appears strongly dose- and duration-dependent, supporting individualized treatment strategies. For patients with contraindications or elevated risk profiles, non-hormonal alternatives such as Selective Serotonin Reuptake Inhibitors (SSRIs), gabapentin, neurokinin receptor antagonists, or local vaginal estrogen therapy offer viable options, though generally with lower overall efficacy for systemic symptoms.

Conclusion: Hormonal replacement therapy effectively relieves moderate to severe menopausal symptoms and prevents fractures, with benefits outweighing risks, as well as dose-duration consequence reduction when started before 60 or within 10 years of menopause. Combined therapy has wider variability if risks compared to estrogen-only therapy, thus individualized risk assessment and guideline-based use are essential to be developed further.

Abstract:
Menopause is a natural stage of ovarian aging marked by the absence of menstruation for 12 consecutive months, usually occurring between 45–55 years of age. Many women experience moderate to severe symptoms that impact their cardiovascular, skeletal, psychological, gastrointestinal and genitourinary systems. Hormone replacement therapy (HRT) is commonly prescribed to relieve these symptoms and to prevent fractures due to osteoporosis. This study reviewed systematic reviews, meta-analyses and major clinical trials that have evaluated the benefits and risks of HRT. Large clinical trials, including the Women's Health Initiative, showed that combined HRT increases risks of breast cancer, stroke, venous thromboembolism, and coronary heart disease. Estrogen-only therapy increased stroke and thromboembolism risk but did not increase breast cancer risk. HRT also demonstrated important benefits, including a 34% reduction in vertebral fractures and 29% reduction in hip fractures. Bone protection was shown to depend on treatment dose and duration, with higher estradiol doses improving bone mineral density significantly. Evidence suggests that starting HRT before age 60 or within 10 years of menopause provides a more favorable risk–benefit balance. Women with contraindications to systemic HRT such as breast cancer may be treated with non-hormonal therapies such as SSRIs, gabapentin, neurokinin receptor antagonists and local vaginal estrogen. In summary, safe and effective management of menopause includes individual risk assessment and treatment based on guidelines.

Key words: Menopause, hormone replacement therapy, estrogen therapy, combined therapy, progesterone therapy, breast cancer, cardiovascular outcomes, non-hormonal therapies, bone mass density.