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THE ROLE AND IMPORTANCE OF HORMONAL DRUGS IN MEDICAL PRACTICE AND THE RELEVANCE OF THEIR IMPROVEMENT

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Abstract. For many years, the primary therapeutic strategy for reducing menopausal symptoms in clinical practice has been hormone replacement therapy (HRT). The majority of the symptoms are genitourinary and vasomotor problems brought on by an estrogen and progesterone shortage. Hormone replacement therapy was first recognized as a universally beneficial and essential intervention, but it later became the focus of intense scientific and clinical controversy, particularly following the release of comprehensive epidemiological studies suggesting possible side effects linked to cancer and cardiovascular risk. By examining its historical development, increased clinical applications, and modifications to guidelines required by recent scientific research, this study seeks to reevaluate the function of HRT in clinical practice. Hormone replacement therapy is the most effective treatment for vasomotor and urogenital symptoms, according to current evidence from clinical research and meta-analyses, which also acknowledges its potential significance in preventing osteoporosis. HRT administration necessitates a thorough individual evaluation that takes into account the patient's age, the time of beginning, and the presence of comorbidities. In this context, the patient's preferences, risk assessment, and the most recent clinical guidelines must all be taken into consideration while making treatment options. In summary, the evaluation of HRT validates its principal function in mitigating menopausal symptoms and emphasizes the necessity of a customized approach that strikes a balance between advantages and disadvantages in order to enhance outcomes for women.

Keywords. Menopause, perimenopause, hormone replacement therapy, menopausal transition, medication interactions, appropriate menopausal care.

Introduction. The goal of hormone replacement therapy for women going through or through menopause is to return their hormone levels to normal. Estrogen and progesterone levels decrease during the menopausal transition and during menopause. HRT is a modern strategy that slows down aging and improves quality of life, thus women going through perimenopause and menopause may find it beneficial. The anti-aging advantages of this therapy are well known. HRT's

main goal is to reduce menopausal symptoms brought on by estrogen insufficiency in the perimenopausal and menopausal stages. Hot flashes, nocturnal sweats, vaginal dryness, mood swings, sleep difficulties, depressive episodes, skin, and metabolic abnormalities are some of these symptoms. Preventing metabolic irregularities in the metabolism of fats and carbohydrates, reducing the risk of cardiovascular disease, and maintaining bone density are all long-term advantages of hormone replacement therapy (HRT). Both the short-term and long-term advantages for the patient as well as the related short-term and long-term hazards must be taken into account while starting HRT [1-5]. The development of hormone replacement therapy is still a hotly contested issue. Endocrinologists Allen and Doisy, who collected estrogen from pregnant women's urine in the 1920s, are credited for clarifying the functions of progesterone and estrogen in female physiology. Understanding the management of the menstrual cycle in women of reproductive age and identifying the alterations that take place throughout menopause were made possible by this ground-breaking work. Edgar Allen and Edward Doisy received the 1943 Nobel Prize in recognition of their contributions to the field of sex hormone research. Twenty years later, conjugated equine estrogens from pregnant mares' urine were used to create the first oral estrogen therapy. The FDA authorized the medication known as Premarin in 1942. Based on results from clinical trials, the use of hormone replacement therapy in clinical practice has given rise to a number of controversial opinions. Concerns have been made about the health dangers connected to its use. Since the Women's Health Initiative (WHI) research data were made public in the early 2000s, the severity of this problem has increased [6-12]. According to the study's findings, postmenopausal women who took combined hormone replacement therapy were more likely to be diagnosed with heart disease, strokes, and breast cancer. The usage of HRT has significantly decreased as a result of these discoveries, and the risk-benefit ratio has been reevaluated. Nevertheless, the study has a number of limitations in spite of the large patient population. The age of the patient at the start of HRT, the length of treatment, and the dosage and mode of administration are important variables. Women over 60 made up the WHI's main cohort, a group linked to higher risks of cardiovascular events and cancer. The significance of starting hormone replacement treatment within ten years of menopause onset is shown by subsequent analyses. More recent research suggests that tiny doses of HRT can be administered safely till death. During menopause, estradiol naturally declines, which has a number of detrimental impacts on metabolism and health. Between 40% and 60% of women seek therapy, and 20% may put it off for more than a year. Vasomotor symptoms (VMS) are still reported by 33% of women aged 65 to 79 and 42% of women aged 60 to 64 [13-20]. According to Australian research, VMS affects 74% of postmenopausal women under 55, with 28% experiencing moderate or severe symptoms. Similar to the stress of unstable housing, these symptoms may have a substantial negative influence on quality of life. In terms of metabolism, the drop in estrogen levels raises the risk of type 2 diabetes by contributing to insulin resistance and increasing central abdominal fat deposition, even in slender women. A more unfavorable lipid profile and compromised endothelial function have an influence on cardiovascular health. Skeletal effects include rapid bone loss beginning prior to the last menstrual cycle, which raises the risk of fractures and may be a factor in sarcopenia, the age-related loss of strength and muscle mass. During perimenopause, some women may have neurological problems with verbal memory, which may get better following menopause [21-26].

The main purpose of the presented manuscript is to provide a brief analysis of the role, importance, and relevance of improving hormonal drugs in medical practice based on the results of authoritative scientific works.

Menopause and the Menopause Transition: An Important Risk Factor and a Physiological Process. Puberty marks the start of the female hormonal cycle, which continues through the reproductive stage and concludes with menopause. This process is continual and always changing. The hypothalamic-pituitary-gonadal axis carefully controls the hormonal pathway. From adolescence until menopause, hormonal changes take place at every stage. The onset of reproductive capacity occurs throughout puberty. Women have regular menstrual cycles with three distinct phases throughout the reproductive phase: luteal, ovulatory, and follicular. The pituitary-ovarian axis and the hormones follicle-stimulating hormone (FSH), luteinizing hormone (LH), estrogen, and progesterone have an impact on these phases. Perimenopause is the stage before menopause. It usually starts in a woman's mid-forties and lasts for four to eight years [6-12]. Hormonal instability, irregular menstruation, anovulatory cycles, and reduced ovarian reserve are signs of this stage. FSH levels rise and estradiol levels fall during perimenopause due to a decrease in inhibin B and anti-Müllerian hormone (AMH). Common symptoms including hot flashes, nocturnal sweats, mood swings, and sleep difficulties are linked to these hormonal shifts. During this shift, up to 80% of women have vasomotor symptoms, such as hot flashes and night sweats. Mood problems and cognitive deficiencies are among the most common psychological symptoms, according to a 2007 study by Freeman and colleagues. The STRAW (Stages of Reproductive Ageing Workshop) framework divides the menopausal transition into two phases: the early phase and the late phase. Changes in the menstrual cycle characterize the early phase, whereas amenorrhea lasting at least sixty days and the absence of menstruation describe the late phase. According to this definition, menopause is defined as the absence of menstruation for a full twelve months without a medical reason. This shift usually occurs in women between the ages of 45 and 55. Menopause is a symptom that the ovaries are no longer able to support reproduction because they are no longer producing eggs [14-24].

A customized approach to patient care is essential to modern medical practice. Despite having comparable clinical symptoms, menopause and the menopausal transition are two different illnesses that may require different treatment approaches. The main cause of the discrepancy is differences in hormone levels, particularly the quantitative needs of the hormones that are the focus of the therapeutic action. The start of hormonal shifts is important, especially in the early stages of menopause, since it affects the different hormonal needs and the extent to which a woman has achieved her reproductive goals. Studies have evaluated the benefit-risk ratio and suggested HRT over time. The guidelines advise taking the lowest effective dose for the shortest period of time to address menopausal symptoms [2-8]. Hormone replacement therapy should be continued by women who have persistent symptoms or are at risk for osteoporosis. Every year, therapy should be reevaluated based on patient preferences, side effects, and clinical symptoms. For women who experience early menopause or premature ovarian insufficiency (POI) as a result of surgery or medical therapies, hormone replacement therapy is advised. Menopausal symptoms are better managed as a result. Oral contraceptives are sometimes used to treat women who are going through an early menopause. For these women, therapeutic intervention should last until the onset of natural menopause. Recognizing that HRT is not a means of contraception is crucial. It is recommended that women using hormone replacement treatment in the early stages of menopause refrain from getting pregnant for the next two years. Pregnancy should be avoided for a year after menopause, according to HRT recommendations for women going through a natural menopause [11-18].

Restoring falling levels of endogenous hormones (estrogen, progesterone, and, in some cases, androgens) is the goal of hormone replacement therapy. For moderate to severe vasomotor symptoms, genitourinary syndrome of menopause, osteoporosis prevention or treatment in high-

risk women, premature ovarian insufficiency or early menopause (under 45 years), and induced menopause (post-oophorectomy), hormone replacement therapy is advised by the NAMS Position Statement and the NICE guidelines. Various combinations of estrogens, progestogens, and sometimes androgens or Selective Estrogen Receptor Modulators (SERMs) are used in hormone replacement therapy. These combinations are created with each patient's unique needs in mind, and they are then customized to satisfy those demands. Menopausal hormones are influenced differently by each hormone [5-11]. The factors that determine the different alternatives for hormone replacement treatment include the particular hormone used, the mode of administration, the patient's age, any comorbidities that may be present, and whether the woman has an intact uterus or has had a hysterectomy. In addition to preventing osteoporosis, estrogen is crucial for controlling vasomotor symptoms such hot flashes, night sweats, and vaginal atrophy. The human body contains three distinct forms of estrogens: conjugated, protein-bound, and free. They are mostly connected to proteins. Just 1% to 2% of them are free estrogen, 38–39% are linked to sex-hormone binding globulin (SHBG), and 60% are linked to albumin. The body produces three main natural estrogens: estriol, 17β-estradiol, and estrone. Although it has little hormonal activity, estriol is a metabolite of both estradiol and estrone. Estriol can be produced from both estradiol and estrone [20-26].

Both oral contraceptives and hormone replacement therapy use progesterone and estrogen, although they differ greatly in terms of target groups, indications, hormonal makeup, and hazards. Clinical decision-making and patient counseling require an understanding of these differences. By inhibiting the hypothalamic-pituitary-ovarian (HPO) axis, oral contraceptives prevent ovulation. Hormone replacement therapy restores endogenous hormone levels without inhibiting the hypothalamic-pituitary-ovarian axis when ovarian function usually stops. To prevent ovulation, oral contraceptives increase levels of synthetic progestins and estrogens, mainly ethinyl estradiol. Hormone replacement therapy uses a progestin, such as micronized or medroxyprogesterone acetate, in combination with lower dosages of natural or bioidentical estrogen, specifically 17-beta estradiol. In women with intact uteri, this treatment focuses on endometrial protection and symptom reduction. Women of reproductive age, particularly those between the ages of 15 and 45, use oral contraceptives to treat hormonal abnormalities or prevent conception. These techniques restrict ovulation and change the endometrial lining and cervical mucus, according to the American Society for Reproductive Medicine Practice Committee. Hormone replacement therapy can be continued when oral contraceptives are used until the start of natural menopause. This depends on the patient's hormonal and physiological conditions [6-17].

The gold standard for reducing cardio-metabolic risk, preventing osteoporosis, and easing menopause symptoms is hormone replacement therapy. Despite the known benefits, using HRT carries some risks, mostly related to endometrial cancer, thrombosis, breast cancer, and stroke. By taking into account the patient's age at the start of HRT, the presence of coexisting conditions, a family history of cancer and thrombotic events, and the length of therapy, the risk can be effectively managed. Prominent professional organizations including NAMS, NICE, and the BMS base their recommendations on this. When starting HRT, a customized approach is crucial. Hormone replacement therapy based on estrogen may have some side effects. Through enterohepatic metabolism, oral estradiol may decrease antithrombin III levels while increasing coagulation factors II, VII, IX, and X. This could double or triple the risk of thrombosis, especially in the first year of treatment [4-12]. Estradiol may be administered transdermally to high-risk patients, such as smokers, obese women, people with thrombophilia, and those with a family history of thrombosis. By optimizing estradiol levels, this technique inhibits hepatic metabolism.

Prothrombotic factors and oral estrogen medication may increase pro-inflammatory variables. Macrovascular issues like myocardial infarction and stroke could result from this. The length of treatment and the date of beginning determine the result. After carefully examining the benefit-risk ratio, relative contraindications provide reevaluation. A migraine is one example, especially if it is accompanied by an aura. It is often linked to premenstrual syndrome and is made worse by the actions of estrogens. In these cases, transdermal treatment at the lowest feasible dosage is more effective than systemic estrogen. When properly controlled, arterial hypertension is a relative contraindication. Some women who take oral estradiol have higher systolic blood pressure. Gallbladder disorders and hypertriglyceridemia are considered relative contraindications. Before beginning hormone replacement medication, a thorough evaluation is necessary because it may make uterine diseases like fibroids and endometriosis worse [16-26].

Discussion. In order to relieve related symptoms, including hot flashes and night sweats, hormone replacement treatment (HRT) replaces women whose ovarian hormones were reduced during the natural menopausal transition. In order to mimic ovarian hormones, traditional HRT usually combines progesterone and estrogen. The FDA-approved hormone replacement therapy (HRT) prevents osteoporosis and relieves severe vasomotor menopausal symptoms. Ethinyl estradiol, conjugated equine estrogen (CEE), synthetic conjugated estrogens, and micronized 17β-estradiol are available estrogen treatments. In individuals with an intact uterus, progesterone is added to assist avoid endometrial hyperplasia. Oral, vaginal, and transdermal administration of systemic hormone replacement therapy (HRT) each have their own advantages and disadvantages. In order to improve patient outcomes, this activity for healthcare professionals aims to improve learners' comprehension of HRT indications, risk-benefit ratios, individualized management, including estrogen and progesterone therapies and administration techniques, and the application of an appropriate interprofessional management approach [2-8]. A cooperative, multidisciplinary strategy is necessary to improve patient-centered treatment, results, safety, and team performance in menopausal HRT. To provide comprehensive care that takes into account each patient's particular needs, doctors, advanced practitioners, nurses, pharmacists, and other health professionals must collaborate. Clinical decision-making is heavily influenced by doctors and advanced practitioners, who use their knowledge of menopause management to customize treatment regimens according to the patient's preferences, symptoms, and medical history. In order to ensure that women are aware of their HRT options, possible side effects, and the significance of follow-up care, nurses play a crucial role in patient education. Pharmacists help by controlling drug interactions, making sure medications are dispensed accurately, and advising patients on how to follow their HRT prescription. Other medical specialists, such dietitians and mental health practitioners, focus on nutrition, emotional health, and lifestyle modifications—all of which are essential elements of comprehensive menopausal care. With customized treatment programs that take into account each woman's risk factors, a patient-centered approach is essential [11-17]. The patient's values and preferences are crucial to the treatment process when the patient and the medical team collaborate to make decisions. Frequent follow-up and monitoring enable therapy modifications, maximizing efficacy and safety. Informed consent, in which patients are given impartial, explicit information regarding the advantages and disadvantages of hormone replacement therapy, is one of the most important ethical factors. In order to guarantee that all women, regardless of background, have access to suitable menopausal treatment, equitable care must be given top priority [22-26].

Conclusions. Many women are experiencing untreated menopausal symptoms as a result of misapplying the findings of a well-designed clinical trial (the WHI trial) to populations and

hormone formulations not included in the study. Additionally, there is widespread confusion among clinicians regarding the true risks and benefits of various hormone therapies. The menopausal transition is not well understood or adequately trained for healthcare workers, and this problem is still mostly unresolved today.

Hormone replacement treatment is considered the gold standard for preventing osteoporosis and treating moderate to severe menopausal symptoms, such as vasomotor and urogenital disorders. Scientific groups continue to have reservations about the use of hormone replacement therapy. Studies conducted in the last few decades have demonstrated significant benefits, particularly when used in a balanced and customized way. It is essential to take into account the timing of beginning, have a thorough awareness of risk factors, and perform continuing prophylaxis in order to guarantee that the advantages of this therapy outweigh its associated risks.

To ensure continuity of care, interprofessional collaboration and communication are essential. Clinicians can ensure patient safety by promptly addressing any difficulties, such as adverse effects or medication interactions, thanks to regular team talks, clear protocols, and unified treatment plans. Results are better, care is safer, and the patient experience is improved when a cohesive team works together and includes the patient at every stage of the decision-making process.

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