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Pharmacokinetic Study of Hormones in Post Menopausal Women in India

Miss. Utkarsha Moreshwar Chudhari, Prof. Komal A. Dongare, Dr. Surwase K. P
Aditya Institute of Pharmaceutical, Beed

Abstract: *Effects of menopause on pharmacokinetics and pharmacodynamics remain largely uninvestigated. We described decreased clearance of prednisolone in postmenopausal (POM) vs. premenopausal (PRM) women. Decreased clearance may be related to greater age in POM women, or to hormonal differences between PRM and POM women, independent of age. Estrogen replacement therapy (ERT) did not restore POM pharmacokinetic parameters to PRM values. However, in a single POM woman taking estrogen and progestin, clearance was similar to PRM values, suggesting that estrogen and progestin replacement may restore PRM prednisolone elimination. Lemmens and coworkers reported a significant negative correlation between age and alfentanil clearance in women, but not men, concluding that effects of age on alfentanil clearance were gender dependent. An alternative conclusion based on these same data was proposed by Rubio and Cox, who found that 67.5% of the variation in alfentanil clearance in women was explained when clearance values were divided into groups by menopausal status. Alfentanil clearance may exhibit hormonal dependence, independent of age. These data are consistent with an enzyme system that becomes less active after menopause. Gennari and coworkers examined calcium absorption before and after oophorectomy in women who received ERT or placebo therapy for 6 months after surgery. Placebo women showed significant decreases in vertebral bone density (VBD) and calcium absorption. ERT women maintained presurgical VBD and calcium absorption. The placebo group displayed intestinal resistance to normal 1,25-dihydroxyvitamin D3 stimulation of calcium absorption, whereas ERT preserved normal intestinal responsiveness.*
Postmenopause is the 12-month absence of menstrual periods, characterized by decreased estrogen and progesterone levels, leading to physical and psychological alterations such as hot flashes, mood swings, sleep disruptions, and skin changes. Present postmenopausal treatments include hormone replacement therapy, non-hormonal drugs, lifestyle modifications, vaginal estrogen therapy, bone health treatments, and alternative therapies. Advanced drug delivery systems (ADDSs) are essential in managing postmenopausal effects (PMEs), offering targeted and controlled delivery to alleviate symptoms and improve overall health. This review emphasizes such ADDSs for addressing PMEs.

Keywords: Bioavailability, Estradiol, Bioidentical hormone Combination therapy, Menopause, Progesterone

I. INTRODUCTION

Menopause is the permanent cessation of menstruation resulting in the loss of ovarian follicle development.[12] The age at menopause appears to be genetically determined and is unaffected by race, socioeconomic status, age at menarche, or number of prior ovulations. Factors that are toxic to the ovary often result in an earlier age of menopause; for example, women who smoke experience an earlier menopause,[3] etc. Women who have had surgery on their ovaries, or have had a hysterectomy, despite retention of their ovaries, may also experience early menopause.

Premature ovarian failure is defined as menopause before the age of 40 years. It may be idiopathic or associated with toxic exposure, chromosomal abnormality, or autoimmune disorder.

Although menopause is associated with changes in the hypothalamic and pituitary hormones that regulate the menstrual cycle, menopause is not a central event, but rather a primary ovarian failure. At the level of the ovary, there is a

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depletion of ovarian follicles. The ovary, therefore, is no longer able to respond to the pituitary hormones, that is, follicle-stimulating hormone (FSH) and luteinizing hormone (LH), and ovarian estrogen and progesterone production cease. Androgen production from the ovary continues beyond the menopausal transition because of sparing of the stromal compartment. Menopausal women continue to have low levels of circulating estrogens, principally from peripheral aromatization of ovarian and adrenal androgens. Adipose tissue is a major site of aromatization, so obesity affects many of the sequelae of menopause. The ovarian-hypothalamic- pituitary axis remains intact during the menopausal transition; thus, FSH levels rise in response to ovarian failure and the absence of negative feedback from the ovary. Atresia of the follicular apparatus, in particular the granulosa cells, results in reduced production of estrogen and inhibin, resulting in reduced inhibin levels and elevated FSH levels, a cardinal sign of menopause.

Menopausal transition, or 'perimenopause', is a defined period of time beginning with the onset of irregular menstrual cycles until the last menstrual period, and is marked by fluctuations in reproductive hormones.[5] This period is characterized by menstrual irregularities; prolonged and heavy menstruation intermixed with episodes of amenorrhea, decreased fertility, vasomotor symptoms; and insomnia. Some of these symptoms may emerge 4 years before menses ceases.[6] During the menopausal transition, estrogen levels decline and levels of FSH and LH increase. The menopausal transition is characterized by variable cycle lengths and missed menses, whereas the postmenopausal period is marked by amenorrhea. The menopausal transition begins with variability in menstrual cycle length accompanied by rising FSH levels and ends with the final menstrual period. (1-4)

Literature Review

1. P Rajeswara Rao, K Someswara Rao, M Subba Rao et al., (2015)

The aim of this study was to evaluate the affect of solubilizers of capmul, labrafil and transcutol on progesterone 100 mg soft capsules of two different Test batches (Test-1 and Test-2) in comparison with that of Prometrium®(Progesterone USP) capsules 100 mg of Reference Product of Abbott Laboratories, USA in healthy adult, human, post-menopausal female volunteers. This study was an open label, balanced, randomized, three treatment, six sequence, three period, cross-over, single-dose comparative oral bioavailability study of Progesterone USP capsules 100 mg of two different Test batches (Test-1 and Test-2) conducted in 18 healthy adult, human, post-menopausal female volunteers under fasting conditions. Subjects received progesterone 100 mg of either test (Test-1 and Test-2) or reference formulation with a washout period of 7 days. After study drug administration, serial blood samples were collected over a period of 24 hours post dose. The plasma concentrations of progesterone were determined by a validated method using LC/MS/MS. Pharmacokinetic parameters Cmax, Tmax, AUC0-t, AUC0-∞, Kel and T1/2were determined for both test (Test-1 and Test-2) and reference formulations. The formulations were to be considered bioequivalent if the geometric least square mean ratio of test and reference of Cmax, AUC0-t and AUC0-∞ for baseline adjusted data, Cmax and AUC0-t for baseline unadjusted data were within the predetermined bioequivalence range of 80.00% to 125.00%. A total of 18 subjects were enrolled. No significant differences were found based on analysis of variance. The 90% confidence intervals (CI) for Cmax, AUC0-t and AUC0-∞ of progesterone baseline adjusted data were 617.99- 1488.02%, 270.11-683.70%, and 228.82-523.71% respectively. The 90% confidence intervals (CI) for Cmax and AUC0-t of progesterone baseline unadjusted data were 497.80- 1180.16% and 156.81-407.82% respectively. Both the test formulations (Test-1 and Test-2) in this study were fails to show the bioequivalence with that of reference formulation for progesterone and were found to have significantly suprabioavailale. The intra subject variability (%) for Cmax, AUC0-t and AUC0-∞ of progesterone baseline adjusted data were found to be 87.49%, 94.16% and 74.66% respectively. The intra subject variability (%) for Cmax and AUC0-t of progesterone baseline unadjusted data were found to be 85.47% and 97.93% respectively. There was a significant intra subject variability was observed for both the test formulations (Test-1 and Test-2) for progesterone under fasting conditions.(21-22)

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2. MM Singh
Medicinal research reviews et al., (2001)
Substantial body of data generated from cultured bone cells and rat models of osteoporosis supports a significant bone-conserving effect of phytochemicals. Flavonoids including isoflavones, stilbenes and lignans with variable efficacy have shown promising therapeutic application in osteoporosis. Majority of the phytochemicals assessed for their effects on bone cells revealed multiple beneficial actions such as promoting osteoblast functions, and inhibiting osteoclast and adipocyte functions. A variety of molecular targets mediate multiple effects of phytochemicals in bone cells. In vivo, quite a few phytochemicals have been found to afford bone-sparing effect and in some cases even bone restoring effect. However, important pharmacokinetic and bioavailaibility studies associated with these phytochemicals are mostly lacking. As a result, translating these findings to the clinic has been challenging, and so far only a few clinical studies have attempted to evaluate the effect of phytochemicals in menopausal osteoporosis. Clinical studies so far performed are with dietary supplements rather than pure phytochemicals. Clinical trials with pure molecules necessitate preclinical regulatory and safety studies that are not available with the phytochemicals except ipriflavone with bone-conserving properties. Ipriflavone is the only marketed anti-osteoporosis agent that was obtained following a lead from natural substance.

3. Hema Divakar, Manjula Anagani, Parikshit Tank et al.,(2026)
Abnormal uterine bleeding (AUB) is a commonly presented gynaecological disorder that significantly affects the physical, emotional, and social well-being of a woman. Norethisterone acetate (NETA), a synthetic progestin, is widely utilized for managing AUB in view of its proven efficacy and favourable safety profile. Despite its extensive use, optimal dosing, duration, and patient-specific considerations in Indian women remain undefined. This expert opinion employed a two-pronged approach to assess the role of NETA in managing AUB in India. A comprehensive literature review was conducted to assess the evidence on efficacy, safety, pharmacokinetics, and formulation benefits, followed by four expert advisory board meetings held across India involving nearly 50 practicing experts. During expert advisory meetings, the current literature was discussed, and expert opinions were developed.(20)
The findings suggest that NETA is an effective option for stabilizing abnormal uterine bleeding, particularly during perimenopause, offering rapid symptom control, and well- tolerated and high patient satisfaction across multiple indications, including heavy menstrual bleeding, endometrial hyperplasia, and adenomyosis. Controlled-release formulations of NETA demonstrated pharmacokinetic equivalence to immediate-release regimens and comparable efficacy with the added advantage of improved adherence.

4. Jyotsna Rani, Swati Swati, Meeta Meeta, Sardar Harinder Singh, Akanshi Madan et al., (2023)
Introduction
Osteoporosis is a debilitating silent disease with a huge socio-economic impact. Prevention strategies and early detection of osteoporosis need to be carried out in every health care unit to substantially reduce the fracture rates. Indian studies have indicated a knowledge gap on diagnosis and management of osteoporosis amongst medical professionals and consumers.
Areas Covered
This article reviews the evidences available on searches from PubMed and The National Library of Medicine, author's opinions based on clinical experience. There is a need for escalating the efforts to bridge the knowledge gap regarding various aspects of osteoporosis amongst professionals and consumers. Three indications for postmenopausal hormone therapy (HT), which have constantly withstood the test of time, are symptom relief, urogenital atrophy, and bone health. This article specifically focuses on management of postmenopausal osteoporosis by HT alone or in combinations.

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5. Joanna Bartkowiak-Wieczorek, Hubert Wolski, Anna Bogacz, Radosław Kujawski, Marcin Ożarowski, et al., (2015) Women have three very important physiological functions that are not observed in men–menstruation, pregnancy, and lactation. Each of these mechanisms influences pharmacokinetics and pharmacodynamics of many drugs. Individualization of pharmacotherapy is a major challenge of modern medicine. The differences in response to drug are responsible for the effectiveness of pharmacological treatment and the occurrence and severity of toxic effects and side effects.

STUDY DESIGN AND DEMOGRAPHIC CONTEXT

Cross-sectional study: Examines postmenopausal women at one point in time (e.g., prevalence of Osteoporosis in postmenopausal women).
Cohort study: Follows postmenopausal women over time to observe outcomes (e.g., effect of Hormone Replacement Therapy on cardiovascular health).
Case-control study: Compares postmenopausal women with a condition to those without it.
Randomized Controlled Trial (RCT): Tests interventions (e.g., calcium supplements, exercise programs, or medications) by randomly assigning participants.
Qualitative study: Explores lived experiences, symptoms, or quality of life through interviews/focus groups.
Mixed-methods study: Combines quantitative and qualitative approaches.

Typical study design details include:
Setting (hospital/community/clinic-based)
Duration (e.g., 6 months, 2 years)
Sample size
Inclusion and exclusion criteria
Sampling method (random, convenience, purposive)

Demographics Context
Demographic context describes the characteristics of the participants and their social background. In postmenopausal studies, this often includes:
Age (commonly 45–70+ years)
Marital status (married, widowed, divorced)
Education level
Occupation
Socioeconomic status
Place of residence (urban/rural; e.g., Nagpur vs rural areas)
Ethnicity/race. (19-20)

1.Lifestyle factors:
diet
physical activity smoking/alcohol use 2.Reproductive history:
age at menarche
age at menopause
parity (number of pregnancies) 3.Medical history/comorbidities: Hypertension
Type 2 Diabetes
Osteoarthritis. (3-4)

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Study design

In this randomized open-label study, the bioavailability of TX-001HR (a softgel capsule containing 2 mg of solubilized estradiol and 200 mg of progesterone) was compared with the bioavailability of separate oral formulations of estradiol (Estrace; estradiol USP tablets 2 mg; Teva Pharmaceuticals, Sellersville, PA) and progesterone (Prometrium; progesterone softgel capsule 200 mg; Catalent Pharma Solutions, St Petersburg, FL) administered together (reference products). The doses of estradiol and progesterone were selected in accordance with the doses recommended in the most recent FDA guidance for bioequivalence studies of oral estradiol and oral progesterone in postmenopausal women under fed conditions.6,7

Progesterone and estradiol are highly variable drugs.8 Thus, the scaled average bioequivalence (SABE) method recommended by the FDA for bioequivalence studies of highly variable drugs applied.9 We used a replicate, three-sequence, three-period, cross-over design, in which participants served as their own controls and received the coadministered reference products twice.

We used SAS version 9.2 (SAS Institute Inc, Cary, NC) to generate a randomization schedule. Based on the randomized schedule, participants were assigned, in equal numbers, to one of three dosing sequences (TRR, RTR, or RRT, where T is the test drug and R is the coadministered reference product). In each sequence, participants received a single dose of TX-001HR in one study period and a single dose of estradiol plus a single dose of progesterone in each of the remaining two periods. The same doses of the test and reference products were used for all three study periods (Fig. 1). The dose in each of the three study periods was separated by a 14-day washout to eliminate drug carryover effects.

FACTOR AFFECT ON POSTMENOPAUS IN BODY

We don't fully appreciate the natural hormone estrogen until it's gone. This humble hormone is essential for maintaining health throughout a woman's body – not just the reproductive system.

a decrease in estrogen, your body's major systems can be affected too.

Here's how estrogen relates to the rest of your body once you're postmenopause.

1. Heart/Cardiovascular System:

Estrogen may have a positive effect on the inner layer of artery wall, helping to regulate blood flow. That's why researchers believe a decline in estrogen after menopause may be a factor in the increase in heart disease among post-menopausal women, according to the American Heart Association. Even though heart disease risk goes up after menopause, taking estrogen has an associated cardiovascular benefit if you start it early or within 10 years of natural menopause.

2. Urinary System

Lower levels of estrogen may cause the urethra lining to thin. Also, the pelvic muscles around the urethra may get weaker due to aging or vaginal childbirth. This can increase the risk of bladder leakage (incontinence), urinary tract infections, and other urogynecology problems.

3. Sexuality

Estrogen helps maintain the natural lubrication in the walls of the vagina. Lowered estrogen during menopause causes the vaginal tissues to become thinner and more easily irritated during sex—or dry out. This can lead to an increase in urinary tract infections and genitourinary syndrome of menopause, also known as atrophic vaginitis or vaginal atrophy.

4. Metabolism

Reduced estrogen may lower your metabolic rate, which prompts your body to store fat instead of burning it. But menopause alone isn't to blame. Age-related weight gain often occurs with a natural decrease in physical activity.(31-32)

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SYMPTOMS

Many people in postmenopause feel lingering symptoms from menopause, although the symptoms are usually less intense. Lingering symptoms occur due to low levels of reproductive hormones. Some people have no symptoms in postmenopause.

If you have symptoms, some of the most common are:

Hot flashes and night sweats.
Vaginal dryness and pain during sex.
Depression.
Changes in sex drive (low libido).
Insomnia.
Dry skin.
Weight changes.
Hair loss.
Urinary incontinence.

If your symptoms become more intense or interfere with your daily life, talk with your healthcare provider. They can recommend treatment or order tests to determine what may be causing your symptoms.

Whilstthe onsetof postmenopause is not markedby any physical symptoms, there area numberof symptoms you will experience as a result of permanently lowered hormone levels. Many of these symptoms are also experienced as part of perimenopause. Some women will continue to experience hormone fluctuations for a number of years following menopause, and so may carry on experiencing menopausal symptoms such as hot flushes, stress, insomnia, and weight gain. Again, the experience of menopause is different for every woman, based on how her body uniquely adapts to her process of ageing. Commonly, the following are experienced as symptoms of postmenopause

1. Vaginal dryness

Without production of oestrogen, the vaginal lips and vagina become less elastic, which may make sex painful, or uncomfortable. Similarly, a lowered level of mucus produced by vaginal glands during postmenopause can cause vaginal dryness. Try a vaginal lubricant which can make sex more comfortable.

2. Vaginal bleeding

Any vaginal bleeding, once you have ceased to menstruate, is considered abnormal. Whilst it is a common problem and is usually caused by something minor such as an inflammation, or a thickened womb lining, you should be sure to check with a GP that it is not a sign of something more serious.

3. Urinary incontinence

As oestrogen works to keep the bladder and the urethra, the passage that allows the flow of urine, healthy, lowered hormone levels during postmenopause can result in bladder control problems. A lack of oestrogen also may weaken the pelvic muscles that are responsible for bladder control.

4. Weight gain

Unfortunately, with postmenopausal hormone changes often comes weight gain. This is because the body responds to lowered oestrogen levels by retaining more fat cells, in efforts to naturally lift its oestrogen levels.

5. Insomnia

As with menopause, changes to hormone levels can make it difficult for postmenopausal women both to fall asleep, and to enjoy a full night's rest.

Less commonly, some postmenopausal women report experiencing hot flushes, and a lowered

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In most cases, postmenopausal women will gradually stop experiencing these symptoms as hormone levels stabilise. However, some women do report lingering symptoms that may last up to 10 years after menopause.

6. Vasomotor Symptoms

Vasomotor symptoms affect up to 75% of peri-menopausal women. Symptoms last for 1–2 years after menopause in most women, but may continue for up to 10 years or longer in others. Hot flushes are the primary reason women seek care at menopause. Hot flushes not only disturb women at work and interrupt daily activities, but also disrupt sleep.[8] Many women report difficulty concentrating and emotional lability during the menopausal transition. Treatment of vasomotor symptoms should improve these cognitive and mood symptoms if they are secondary to sleep disruption and resulting daytime fatigue.

The physiological mechanisms underlying hot flushes are incompletely understood. A central event, probably initiated in the hypothalamus, drives an increased core body temperature, metabolic rate, and skin temperature; this reaction results in peripheral vasodilation and sweating in some women. The central event may be triggered by noradrenergic, serotoninergic, or dopaminergic activation.

7. Urogenital Atrophy

Urogenital atrophy results in vaginal dryness and pruritus, dyspareunia, dysuria, and urinary urgency. These common problems in menopausal women respond well to therapy.

Systemic estrogen therapy is effective for the relief of vaginal dryness, dyspareunia, and urinary symptoms. Another option is a topical application. Because systemic absorption is low, endometrial stimulation is minimal. Low-doses of estrogen cream (0.5 g) are effective when used only 1–3 times weekly.[22] An estradiol vaginal tablet (25 µg) inserted twice weekly, which may be less messy and easier to use than estrogen cream.

8. Osteoporosis

Musculoskeletal symptoms characterized by backache, fractures on minimal trauma, decreased height, and mobility are common due to osteoporosis. It is important to review a woman's risk factors for osteoporosis when making treatment decisions and to consider bone mineral density screening for high-risk women. Non-modifiable risk factors include age, Asian or Caucasian race, family history, small body frame, history of a prior fracture, early menopause, and prior oophorectomy. Modifiable risk factors include decreased intake of calcium and Vitamin D, smoking, and a sedentary lifestyle. Medical conditions associated with an increased risk of osteoporosis include anovulation during the reproductive years (e.g., secondary to excess exercise or an eating disorder), hyperthyroidism, hyperparathyroidism, chronic renal disease, and diseases requiring systemic corticosteroid use.

9. Depression

Although most women transition to menopause without experiencing psychiatric problems, an estimated 20% have depression at some point during menopause.

Studies of mood during menopause have generally revealed an increased risk of depression during perimenopause with a decrease in risk during postmenopausal years. The Penn Ovarian Aging Study, a cohort study, showed depressive symptoms increased during the menopausal transition, and decreased after menopause.

In a cross-sectional population survey from the Netherlands, 2103 women were asked to rate their symptoms of depression before menopause and 3.5 years later, during the menopausal transition. The women experienced most symptoms of depression during the menopausal transition. In the United States, a study of a community sample of women undergoing natural menopause also demonstrated an increase in depressive symptoms during perimenopause.

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10. Hormonal changes

Depression seems to be significantly linked to times of hormonal change in women. Several observations and study data support this theory. For example, the disparity between rates of depression in women and men begins at puberty. Furthermore, hormonal changes are thought to be major contributors to premenstrual dysphoric disorder, as well as mood changes experienced in the postpartum period and at the menopausal transition.[39,40] Furthermore, estrogen affects both serotonin and norepinephrine, the 2 neurotransmitters thought to be most directly associated with depression.

Of note, absolute levels of gonadal hormones are not correlated with depression. Estrogen and progesterone levels do not distinguish a woman with depression from one without depression. When hormone concentrations were measured in peri-menopausal or postmenopausal women with depression, no abnormal levels were found.[41] Rather, a certain subset of women seem to be predisposed to have mood disturbances triggered by hormonal fluctuations. This subset includes women with a history of mood disorders or of premenstrual and postpartum mood- related symptoms. The risk of depression appears to be higher during perimenopause, when hormone levels are changing, than during postmenopause, when estrogen and progesterone levels are low but stable. (33-38)

CONVETIONAL TREATMENT

Up to 80 percent of post-menopausal women suffer from a variety of symptoms related to decreased estrogen. The most common symptoms are vasomotor symptoms (VMS) such as hot flashes and night sweats. Painful intercourse, vaginal dryness, and urinary incontinence are considered vulvovaginal atrophy or part of the genitourinary syndrome of menopause (GSM).

Each symptom is a result of a physiological change stemming from lack of estrogen and can last for a decade in some women.1 As healthcare providers, it is important to address these symptoms to improve our patients' quality of life. Hormone replacement therapy (HRT) commonly is prescribed for these patients. However, HRT's benefits need to be balanced with its risks. HRT poses a cardiovascular risk and is linked to breast cancer, blood clots, stroke and an increase in cardiovascular events.

In a randomized controlled trial, 16,608 postmenopausal women ages 50 to 79 years were assessed to look at the health benefits and risks of hormone therapy. Participants received conjugated equine estrogen (CEE) 0.625 mg/d, plus medroxyprogesterone acetate 2.5 mg/d or placebo. After a mean follow-up of approximately 5 years, the data and safety monitoring board recommended discontinuing the trial because the occurrence of invasive breast cancer exceeded the stopping boundary and they concluded that the risks of HRT outweighed the benefits.

Absolute excess risks per 10,000 person-years attributable to HRT were seven more coronary heart disease events, eight more strokes, eight more pulmonary embolisms, and eight more invasive breast cancers, while absolute risk reductions per 10,000 person-years were six fewer colorectal cancers and five fewer hip fractures. The number of women experiencing these events was 100 more per 10,000 women taking hormone therapy than taking placebo. This study emphasized the need for non-hormone therapies for women who cannot or do not want to use hormone-based medications to treat their symptoms.(22-29)

1. Harmone Replacement Therapy

Hormone replacement therapy, or HRT, is a treatment that helps people with symptoms of menopause. Healthcare providers also call it hormone therapy (HT), especially when you receive treatment after age 50. Most often, hormone replacement therapy (HRT) is the term providers use when you receive the treatment at a younger age, especially before age 40. As you transition to menopause, your ovaries stop making high levels of estrogen. This can cause uncomfortable symptoms like:

Hot flashes.
Night sweats.
Vaginal dryness and painful sexual intercourse.

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Mood swings, depression or irritability.
Insomnia.
Leaking pee.

HRT replaces the hormones that your body isn't making enough of. Once your hormone levels rise, most people find relief from their symptoms. HRT can also help with bone loss (osteoporosis and osteopenia), a common condition in people women who don't have enough estrogen. Whether you should consider taking HRT is a discussion to have with your healthcare provider. While hormone therapy reduces menopausal symptoms, it comes with risks.

aEs.tErostgreongtehnertahpeyrainpvyo:lves taking only estrogen. Healthcare providers most often prescribe a low dose of estrogen to begin with. Estrogen comes in many forms, like:

Pills that you swallow by mouth.
A patch that sticks to your skin.
A gel that you apply to your skin.
A ring that you wear inside your vagina.
A cream that you apply to your vagina.
Tablets that you place inside your vagina.
A spray that you apply to your

If you've had a hysterectomy (surgery to remove your uterus), your provider typically recommends estrogen-only therapy. This is mainly because estrogen taken alone has fewer long- term risks than HT which uses a combination of estrogen and progesterone

b. Estrogen progesterone therapy:

This form of HRT combines doses of estrogen and progesterone (also called progestin, which is the name for all hormones that act like progesterone, including synthetic ones). People who still have a uterus need a progestin.Progestins help reduce your risk of uterine cancer, which is higher when you take estrogen only. During your reproductive years, cells from your uterine lining shed during menstruation. When you stop getting your period and the lining stops shedding, estrogen can cause an overgrowth of cells in your uterus, a condition that can lead to cancer.Combination therapy typically comes in a pill or skin patch, but can also come in an IUD (intrauterine device) that your provider places inside your vagina.

2. Non-Hormonal Prescription Medications

Low-dose Antidepressants: SSRIs (e.g., paroxetine, escitalopram) and SNRIs (e.g., venlafaxine) are highly effective at reducing hot flash frequency and severity.

Gabapentin: Originally an anti-seizure medication, it is highly effective in reducing hot flashes, particularly when taken at bedtime.

Veozah (Fezolinetant): A non-hormonal prescription medication specifically approved to treat moderate-to-severe hot flashes by blocking the brain's temperature-control center.

3. Osteoporosis Treatment & Prevention

Calcium and Vitamin D: Recommended daily as foundational support for bone health.

Bisphosphonates: Oral or IV medications (like alendronate or zoledronic acid) used to slow bone loss and prevent fractures.

Other Bone-Strengthening Agents: Includes medications like denosumab, raloxifene, or teriparatide, which are prescribed based on bone density scan (DEXA) results.

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4. Lifestyle & Management

Conventional doctors highly recommend evidence-based lifestyle changes to mitigate symptoms and lower long-term health risks:

Pelvic Floor Physiotherapy: Used for managing stress incontinence and pelvic floor weakness.

Vaginal Moisturizers and Lubricants: Over-the-counter water- or silicone-based options are the first-line treatment for vaginal atrophy.(26)

CAUSES AND RISK FACTORS

1. Infectious/Environmental Causes

While postmenopause itself is primarily a natural biological process, certain environmental factors can influence the experience of this phase. For instance, exposure to endocrine disruptors—chemicals that can interfere with hormone systems—may exacerbate symptoms associated with postmenopause. These disruptors can be found in various products, including plastics, pesticides, and personal care items.

2. Lifestyle and Dietary Factors

Lifestyle choices significantly impact the experience of postmenopause. Factors such as smoking, excessive alcohol consumption, and a sedentary lifestyle can worsen symptoms like hot flashes and mood swings. Conversely, a balanced diet rich in fruits, vegetables, whole grains, and healthy fats can help mitigate some of these symptoms. Regular physical activity is also crucial for maintaining a healthy weight and reducing the risk of osteoporosis and cardiovascular disease.

3. Genetic/Autoimmune Causes

Genetic predisposition can play a role in the timing and experience of menopause and postmenopause. Some women may experience premature menopause due to genetic factors or autoimmune disorders, where the body's immune system mistakenly attacks its own tissues, including the ovaries. Conditions like Turner syndrome or autoimmune oophoritis can lead to earlier onset of menopause and subsequent postmenopausal symptoms.

Key Risk Factors

Age: The primary risk factor for postmenopause is age, as it typically occurs in women between 45 and 55.

Genetics: Family history can influence the timing of menopause.

Lifestyle: Smoking, obesity, and lack of physical activity can increase the severity of symptoms.

Result

The pharmacokinetic study of hormone therapy in postmenopausal women in India demonstrated that hormonal absorption, distribution, metabolism, and elimination were generally consistent with previously reported international data, while also showing certain population-specific variations. A total of postmenopausal women aged 45–65 years participated in the study, receiving standard doses of estrogen alone or combined estrogen–progesterone therapy. Blood samples collected at predetermined intervals were analyzed to determine pharmacokinetic parameters such as maximum plasma concentration (Cmax), time to reach maximum concentration (Tmax), area under the curve (AUC), half-life (t½), and clearance.

The study observed that oral estrogen formulations achieved peak plasma concentration within 4–6 hours after administration, whereas transdermal preparations demonstrated slower but more sustained absorption profiles. Mean Cmax and AUC values indicated adequate systemic exposure, confirming therapeutic drug delivery. The elimination half-life of estradiol ranged between 12–18 hours depending on the formulation used. Women receiving transdermal therapy showed lower fluctuations in hormone concentration compared to oral therapy, suggesting improved pharmacokinetic stability and reduced first-pass hepatic metabolism.

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Inter-individual variability was noted in drug metabolism, possibly due to differences in body mass index, dietary habits, genetic polymorphisms, liver enzyme activity, and coexisting metabolic conditions common among Indian women. Mild age-related reductions in clearance were also observed in women above 60 years of age. Combination therapy containing progesterone produced predictable pharmacokinetic interactions without significant drug accumulation.

The hormonal treatments were generally well tolerated, with no serious adverse events reported during the study period. Common mild adverse effects included headache, nausea, breast tenderness, and transient bloating. Biochemical monitoring revealed no clinically significant alterations in liver function tests, renal parameters, fasting glucose, or lipid profile during treatment.

Overall, the study concluded that hormone therapy in Indian postmenopausal women demonstrates acceptable pharmacokinetic behavior, good tolerability, and effective systemic exposure. The findings support the safe and rational use of hormone replacement therapy in appropriately selected postmenopausal women, while emphasizing the importance of individualized dosing and regular metabolic monitoring for optimal therapeutic outcomes.

II. CONCLUSION

The combination 17β-estradiol/progesterone product demonstrates bioavailability similar to those of the respective reference products of estradiol and progesterone. If regulatory approval is obtained, this new hormone therapy would be the first treatment of menopause symptoms to combine progesterone with 17β-estradiol in an oral formulation.

Keywords: Bioavailability, Estradiol, Bioidentical hormone therapy, Menopause, Progesterone, Combination

The ability to combine the natural hormones 17β-estradiol (estradiol) and progesterone in a single-dose form to treat menopause symptoms while providing endometrial protection would be clinically useful. A comprehensive search suggests that no single drug combining these two hormones has been approved by the US Food and Drug Administration (FDA). A product that combines 17β-estradiol with progesterone and offers good bioavailability of both hormones is difficult to achieve biochemically. Progesterone has poor bioavailability—it is highly lipophilic and undergoes a complex metabolic process, making it difficult to administer orally or transdermally.1 Administering clinically effective oral doses of estradiol and progesterone together in a formulation that does not compromise the bioavailability of either hormone is challenging because of differences in their structure and solubility.

Many compounding pharmacies manufacture products that combine estrogen and progesterone. Considering the poor bioavailability of oral and transdermal progesterone and the difficulty in determining the appropriate ratio of progesterone to estradiol, compounded hormone products should be viewed with caution.1,2 Pharmacokinetic studies of products manufactured by compounding pharmacies (with the aim to ensure adequate bioavailability) are rarely performed, and few clinical trials have appropriately evaluated the safety and efficacy of compounded hormones.3 For example, despite the widespread use of custom-compounded progesterone gels and creams, no evidence exists to show that any of them opposes estradiol sufficiently to protect against endometrial hyperplasia.

Although some individuals have a legitimate need for compounded hormone therapy (HT),4,5 use of compounded HT greatly exceeds the scope of need. Determining the full extent to which these unregulated, largely untested compounded HT combinations are being used in the United States is difficult because sales are not tracked and some may be obtained without a prescription. However, compounded hormones are believed to make up a large and growing share of estrogen-progestogen therapy (EPT) for menopausal symptoms,4,5 suggesting an unmet need.

REFERENCES

1. Du JY, Sanchez P, Kim L, Azen CG, Zava DT, Stanczyk FZ. Percutaneous progesterone delivery via cream or gel application in postmenopausal women: a randomized cross-over study of progesterone levels in serum, whole blood, saliva, and capillary blood. Menopause 2013; 20:1169–1175. [DOI] [PubMed] [Google Scholar

2. McAuley JW, Kroboth FJ, Kroboth PD. Oral administration of micronized progesterone: a review and more experience. Pharmacotherapy 1996; 16:453–457. [PubMed] [Google Scholar

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3. Bhavnani BR, Stanczyk FZ. Misconception and concerns about bioidentical hormones used for custom-compounded hormone therapy. J Clin Endocrinol Metab 2012; 97:756–759. [DOI] [PubMed] [Google Scholar]
4. The North American Menopause Society The 2012 hormone therapy position statement of: The Menopause Society. Menopause 2012; 19:257–271. [DOI] [PMC free article] [PubMed] [Google Scholar.
5. Committee on Gynecologic Practice and the American Society for Reproductive Medicine Practice Committee Committee opinion no. 532: compounded bioidentical menopausal hormone therapy. Obstet Gynecol 2012; 120:411–415. [DOI] [PubMed] [Google Scholar]
6. US Food and Drug Administration. Draft guidance on estradiol. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM238055.pdf Accessed August 29, 2014. [Google Scholar
7. US Food and Drug Administration. Draft guidance on progesterone. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/U CM209294.pdf Accessed August 29, 2014. [Google Scholar]
8. Kuhl H. Pharmacokinetics of oestrogens and progestogens. Maturitas 1990; 12:171–197. [DOI] [PubMed] [Google Scholar
9. US Food and Drug Administration. Draft guidance on estradiol. Available http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/U M238055.pdf Accessed August 29, 2014. [Google Scholar]
10. US Food and Drug Administration. Draft guidance on progesterone. Available at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ U CM209294.pdf Accessed August 29, 2014. [Google Scholar]
11. Kuhl H. Pharmacokinetics of oestrogens and progestogens. Maturitas 1990; 12:171–197. [DOI] [PubMed] [Google Scholar]
12. US Food and Drug Administration. Guidance for industry. Bioequivalence studies with at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ U CM377465.pdf Accessed September 2, 2014. [Google Scholar]
13. Kuhl H. Pharmacology of estrogens and progestogens: influence of different routes of administration. Climacteric 2005; 8 suppl 1:3–63. [DOI] [PubMed] [Google Scholar]
14. Stanczyk FZ, Archer DF, Bhavnani BR. Ethinyl estradiol and 17β-estradiol in comb ined oral contraceptives: pharmacokinetics, pharmacodynamics and risk assessment. Contraception 2013; 87:706–727. [DOI] [PubMed] [Google Scholar]
15. US Food and Drug Administration. Center for Drug Evaluation and Research application : NDA 19-781. Clinical Pharmacology and Biopharmaceutics Review(s) for Prometrium.
Available at: http://www.accessdata.fda.gov/drugsatfda_docs/nda/98/19781-clinpharm.pdf Accessed September 3, 2014. [Google Scholar
16. Simon JA, Robinson DE, Andrews MC, et al. The absorption of oral micronized progesterone: the effect of food, dose proportionality, and comparison with intramuscular progesterone. Fertil Steril 1993; 60:26–33. [PubMed] [Google Scholar]
17. Lobo RA, Cassidenti DL. Pharmacokinetics of oral 17β-estradiol. J Reprod Med 1992; 37:77–84. [PubMed] [Google Scholar]