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Review Article

Beyond the Hot Flashes: Exploring the Holistic Approaches to Menopause Management – A Review

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Abstract
The menopause represents a natural phase in the female life cycle rather than a pathological condition. From an evolutionary perspective, this physiological transformation signifies a crucial reproductive shift occurring in mid-life. Defined as the point at which ovarian function terminates, menopause leads to the cessation of menstruation, decline in ovarian follicular activity, and notable reduction in levels of estrogen and progesterone hormones. This literature review aims to explore recent advancements in menopause research concerning pharmaceutical interventions, innovative treatments, as well as the nuances of hormonal replacement therapy (HRT) and complementary and alternative medicine approaches. It seeks to pinpoint gaps in current knowledge to guide future investigations, focusing on key themes such as Hormone Therapy, Hypnosis, Aromatherapy, Phytoestrogens, and Reflexology. The systematic review involved an exhaustive online search across various databases including PubMed, CINAHL, MEDLINE, Science Direct, Scopus, and Web of Science. The ultimate compilation comprises 34 scholarly articles, along with 21 supplementary articles pertaining to the subject matter. Various treatment modalities, including hormonal (MHT) and non-hormonal alternatives, are available for alleviating menopausal symptoms. The ongoing refinement of clinical knowledge will enhance the therapeutic efficacy and the judicious management of patient care. Additional research endeavors are warranted concerning menopause and its associated treatment modalities.

Key words: Aroma therapy, Hormone Therapy, Hypnosis, Phytoestrogens Reflexology

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INTRODUCTION

Menopause signifies the termination of menstrual bleeding, a term originating from the Greek words meno, meaning "month or menses", and pausis, meaning "pause". It denotes the permanent halt of menstruation due to the decline in ovarian function at the culmination of the reproductive phase **(DC Dutta –2020).** Menopause is a natural physiological occurrence in the life of women, representing an inevitable aspect of the aging process involving the cessation of ovarian reproductive capability either spontaneously or due to underlying conditions.

According to the **World Health Organization (2022)** Menopause fact sheet, there are approximately 985 million women aged over 50 globally, constituting 26% of the female population; these figures are projected to increase in the coming decades owing to enhanced longevity, thereby prompting the WHO to prioritize women's health on a global scale.

The age at which menopause commences can vary, with the typical onset falling between 45 and 55 years. The average age for menopause is generally around 51 years, although it can occur anytime from a woman's 30s to the mid-50s or beyond.

Several factors, such as a history of treated depression, exposure to harmful substances, epilepsy, pelvic radiation during childhood cancer treatment, smoking, and poor dietary intake, have been associated with an earlier onset of menopause. Additionally, women who have not undergone childbirth tend to experience menopause at a younger age, while those who are overweight often reach menopause later in life, according to **(Shaikh Zinnat Ara Nasreen, Management of menopause-2022)**

India, boasting a populace of 1.2 billion individuals, stands as the second largest burgeoning economy and the second most densely inhabited nation globally. As reported in the most recent data by the World Health Organization (WHO) in 2018, the life expectancy for females in India stands at 70.3 years, with a projected increase to 77 years by 2050 **(Hill K., 1996).** A substantial portion, amounting to 60%, of the total fatalities in India can be attributed to non-communicable diseases. Presently, a segment constituting about 10% of India's inhabitants, surpassing 100 million individuals, is aged over 50 years.

A study conducted **by Peeyananjarassri (2006)** involved 270 women aged between 45 and 65 years, who sought medical attention at the gynecological and menopause clinic in Songklanagarind Hospital. The mean age at menopause among the postmenopausal women was determined to be 48.7 years, with a range spanning from 40 to 57 years. The prevalence rates for typical menopausal symptoms like hot flushes, night sweats, and vaginal dryness among women aged 45-65 years were found to be 36.8%, 20.8%, and 55.3%, respectively **(Gartoulla, P., et al., 2015).** In the current investigation, prevalent symptoms included emotional disturbances at 90.7%, headaches at 72.9%, lethargy at 65.4%, and dysuria at 58.9% **(Duffy, O. K. et al., 2012).** India, boasting a populace of 1.2 billion individuals, stands as the second largest burgeoning economy and the second most densely inhabited nation globally.

MANAGEMENT OF MENOPAUSE

Management of menopause entails the consideration of Hormone Therapy. The pharmacotherapy options for menopause can be categorized into hormonal and nonhormonal therapy. Menopause hormone therapy (MHT), also known as hormone replacement therapy (HRT), encompasses a range of preparations containing sex hormones that are administered in cases characterized by low levels of oestrogen. Oestrogen-only therapy is identified as oestrogen replacement therapy (ET, ERT), whereas the combination of oestrogens and progestogens is referred to as estrogen-progestogen therapy (EPT). It is crucial to differentiate between these therapies due to the significant variations in their benefit-risk ratio.

HORMONE REPLACEMENT THERAPY AND ITS TYPES:

The various types of Hormone Replacement Therapy can be outlined as follows: Oestrogen-only Therapy: According to de Villiers, T. J et al (2013), Oestrogen-only MHT (oestrogen therapy) is utilized for women who have undergone hysterectomy. The human body produces three types of oestrogen that can be supplemented. Estrone (E1), predominantly synthesized in fat tissue, stands as the primary type of oestrogen found in the body post-menopause. Estradiol (E2), the most potent estrogen, is naturally occurring in the body pre-menopause and is produced by the ovaries, with its levels decreasing significantly post-menopause.

The standard starting doses encompass: Conjugated equine estrogen 0.45 to 0.625 mg orally daily, Micronized 17β-Estradiol 0.5 to 1 mg orally daily, 17β-Estradiol 0.0375 to 0.075 mg per day transdermal patch, Estradiol 10 mcg intravaginally (The NAMS 2017 Hormone Therapy Position Statement Advisory Panel, 2017). The initiation of systemic estrogen therapy necessitates an evaluation of the available preparations in terms of types and regimens. The choice of the preferred regimen is guided by underlying health concerns and personal preferences. The therapeutic use of estrogens effectively alleviates nearly all climacteric symptoms and serves as a proficient strategy for the prolonged prevention of estrogen deficiency and certain other conditions where a direct correlation may not be immediately apparent **(Archer DF et al, 2011).**

BENEFITS OF HORMONE REPLACEMENT THERAPY:

The vasomotor symptoms (VMS) in menopause have been linked to sleeping disorders, concentration issues, decreased quality of life, and elevated cardiovascular risk, as well as impacts on cognitive functions and bone density. These symptoms typically persist for an average of 7.4 years. Hormone replacement therapy (HRT) has been shown to be beneficial in addressing chronic insomnia. The positive influence of oestrogens on sexual function is attributed to the resolution of vulvovaginal atrophy (VVA) and the alleviation of VMS.

RISKS OF HORMONE REPLACEMENT THERAPY:

The risks associated with hormone replacement therapy (HRT) are influenced by several factors including the type of hormones used, dosage, and method of administration, treatment duration, and the age of the individual. Side effects such as mastodynia, fluid retention, nausea, lower limb cramps, and headaches may manifest during estrogen therapy. Studies like the Women's Health Initiative (WHI) have indicated heightened risks of breast cancer and cardiovascular events with the oral intake of estrogens and medroxyprogesterone acetate. Oral forms of HRT, whether estrogens-only or combined with progesterone, elevate the risk of thromboembolic events, particularly stroke in older women who commence therapy more than a decade post-menopause. Combination therapy of oestrogen and progesterone marginally increases the risk of breast cancer, especially with synthetic progestins like medroxyprogesterone acetate. While HRT slightly raises the likelihood of gallbladder disease, the overall risk remains low, as noted by **Lobo R. A. (2013).**

ROUTE OF ADMINISTRATION:

Oestrogens can be administered through various routes including oral, transdermal, percutaneous, intramuscular, intranasal, subcutaneous, or local (vaginal) methods, with dosages and timings customized for each patient. Transdermal administration is favored in cases of intolerance to oral treatment, impaired liver function, hypertriglyceridemia,

diabetes mellitus, and susceptibility to thromboembolic disorders. By circumventing the first-pass effect observed in oral administration, transdermal delivery offers improved bioavailability, helps maintain a steady balance of estrogen levels over the long term, and supports the physiological ratio of estradiol and estrone levels.

According to Fait T et al. (2018), metered-dose transdermal spray (EMDTS) is the newest way of delivery. In a recent study, the number of EMDTS 1.53 mg dosages in symptomatic menopausal women was associated with a rise in serum levels of estradiol, estrone, and estrone sulfate. After one puff, the maximum levels were 36 pg/mL of estradiol and 50 pg/mL of estrone; after three puffs, the levels were 54 pg/mL and 71 pg/mL. It took 18 to 20 hours after application to reach the maximum estradiol concentration. On the seventh and eighth day of application, a stable level was attained. Transdermal estrogen spray offers the benefit of precision dosing along with the safety of transdermal application.

HORMONAL THERAPY FOR WOMEN WITH A UTERUS:

For women who still have a uterus, hormonal therapy with both estrogen and progestogen is recommended. This is especially true for those who have had their endometrium (the lining of the uterus) removed through endometrial ablation, as the risk of endometrial cancer remains. Therefore, it's advised to use hormonal therapy with both estrogen and progestogen to protect against endometrial cancer in women with a uterus. However, it's important to note that hormonal therapy, specifically those with estrogen, can increase the risk of breast cancer over a period of 3 to 5 years. Thus, it's currently suggested that doctors only prescribe hormonal therapy for women with a uterus to manage menopausal symptoms like hot flashes and vaginal dryness, using the lowest effective dose for the shortest duration possible. To address vaginal dryness, estrogen can be directly applied to the vagina using a vaginal cream. This method delivers a minimal amount of estrogen, which is absorbed by the vaginal tissues, effectively treating vaginal dryness. **(Sood R., Faubion et al. 2014)**

CONTRAINDICATIONS FOR HORMONAL THERAPY FOR MENOPAUSE:

Hormonal therapy, which includes both oral and transdermal estrogen, comes with several contraindications as outlined by **Davis SR et al (2023) and Baber RJ et al (2016).** These contraindications are related to the potential adverse effects and the relative toxicity of oestrogen-based therapies.

Breast cancer that is current, historical, or suspected, Cancer affecting the endometrium, Arterial thromboembolic disease that is either active or has occurred recently, such as angina or myocardial infarction, Previous venous thrombosis of unknown cause, specifically deep vein thrombosis or pulmonary embolism, Disease of the coronary arteries, A medical condition characterized by a sudden loss of brain function, Acute dysfunction of the liver, A type of porphyria known as Porphyria Cutanea Tarda, Abnormal bleeding from the genital area that has not been diagnosed, The state of being pregnant, High levels of triglycerides in the blood, Benign tumors in the uterus, Sensitivity to the active components of the treatment, High blood pressure that is not being treated are considered as absolute contraindications for Hormone replacement Therapy. Contraindications related to estrogen administration transvaginally, such as creams or suppositories, are not applicable due to the insufficient serum concentration of estrogen through this route to elicit any physiological impact.

Non-Hormonal Therapy:

The climacteric syndrome can also be managed without the use of hormones. While the medications utilized may alleviate symptoms related to acute oestrogen deficiency to some degree, their impact on long-term alterations resulting from oestrogen insufficiency remains unverified.

A) Low-dose Antidepressants: Selective serotonin reuptake inhibitors have demonstrated efficacy in treating depression during perimenopause, with some offering slight relief for hot flashes. For individuals unable to undergo oestrogen therapy due to health concerns or requiring antidepressants for mood disorders, a low-dose antidepressant like fluoxetine or sertraline could be beneficial. Paroxetine mesylate (Brisdelle) was approved by the FDA in June 2013 as the initial nonhormonal treatment for vasomotor symptoms associated with menopause.

B) Gabapentin (Neurontin): Despite being primarily prescribed for seizures, gabapentin has displayed effectiveness in reducing hot flashes. It is particularly useful for women who are unsuitable for oestrogen therapy and those experiencing nocturnal hot flashes. The recommended dosage of gabapentin is 300 mg three times daily for alleviating menopausal hot flashes and mood disturbances.

C) Ospemifene (Osphena): This medication, resembling oestrogen but not classified as such (acting as an oestrogen agonist/antagonist with tissue-selective effects), is administered orally once daily. While it aids in relieving vaginal dryness stemming from menopause, it may also induce hot flashes. Ospemifene is intended for women encountering challenges with vaginal oestrogen usage or opting against vaginal medications.

Complementary and Alternative Medicine for Menopause

As delineated by the **National Center for Complementary and Integrative Health in 2017**, complementary and alternative medicine encompasses mind-body practices (such as hypnosis, cognitive-behavioral therapy, relaxation, biofeedback, meditation, and aromatherapy), natural products (including herbs, vitamins, minerals, and dietary supplements), and whole-system approaches (like traditional Chinese medicine, reflexology, acupuncture, and homeopathy).

HYPNOSIS

Hypnosis, a mind-body intervention characterized by a deeply relaxed state of concentrated attention, personalized mental imagery, and suggestion, has been explored for managing menopausal symptoms.

In a randomized controlled trial conducted by **Elkins, G. R., Fisher et al. in 2013**, involving 187 women, the effectiveness of hypnosis was compared to an active structured attention control, resulting in a notable reduction in subjective hot flash frequency (74%), interference (80%), and physiologically monitored hot flashes (57%), as per **Johnson AK (2016).**

COGNITIVE BEHAVIORAL THERAPY:

Cognitive-behavioral therapy (CBT), a therapeutic approach combining cognitive and behavioral strategies, has been widely utilized for addressing symptoms like hot flashes, depression, and other manifestations associated with menopause. Known for its time-limited nature, CBT aims to alter cognitive assessments and behavioral patterns to alleviate symptoms. The intervention may encompass educational sessions, motivational dialogues, relaxation techniques, controlled breathing exercises, and other methods aimed at improving symptoms. Studies by **Samami E et al. in 2022** and **Tremblay, A. et al. in 2008** have suggested that cognitive behavioral therapy and relaxation techniques hold promise for alleviating vasomotor symptoms and hot flashes in healthy postmenopausal women.

AROMATHERAPY

Aromatherapy is described as "the scientific utilization of highly concentrated essential oils or essences obtained from plants to harness their therapeutic attributes". Essential oils, with various application methods, are capable of directly accessing the neocortex section of the brain by means of connections that extend to the limbic system and the hypothalamus via scent.

The use of Aromatherapy can have a positive influence on the immune system by ameliorating mood, boosting brain function, and augmenting other vital biological processes crucial to health and recovery.

In a study conducted by **Darsareh F, Taavoni S, Joolaee S, and Haghani H. in 2013**, a randomized clinical trial was carried out to assess the impact of aromatherapy massage on psychological symptoms in menopause. The findings indicated that both aromatherapy massage and regular massage were effective in decreasing psychological symptoms, with aromatherapy massage showing a greater efficacy than the standard massage.

Chien and colleagues in **2012** discovered that 12 weeks of inhaling lavender led to improved self-reported sleep compared to a control group receiving health education. Through a double-blinded 12-week clinical crossover trial involving 100 women, it was observed that lavender essential oil reduced hot flashes by 50%, a notably higher percentage in comparison to the <1% reduction witnessed in the placebo (diluted milk) control group.

PYTOESTROGENS:

Phytoestrogens, also known as plant oestrogens, are non-steroidal compounds that include flavones, lignans, and Coumestans. The presence of phytoestrogens and Phyto progesterone's in medicinal plants, alongside the antiandrogenic effects of these plants, hinder the conversion of testosterone to dihydrotestosterone and promote the conversion of testosterone and androstenedione to oestrogen in peripheral tissues, thereby mitigating menopausal symptoms. Various studies have highlighted the reduction in menopausal symptoms among Asian women due to regular consumption of phytoestrogens in their diet, as noted by **Geller, S. E., & Studee**, **L. (2006) and Ciotta, L., et al. (2012)** suggesting that isoflavones can serve as an alternative to hormone-replacement therapy.

A comprehensive analysis of 23 randomized controlled studies concluded that certain plant-based substances known as phytoestrogens are likely to have positive effects on bone health among menopausal women. This conclusion was drawn by **Adlercreutz, H., et al**. in **1997** through a series of studies collectively known as a meta-analysis. Specifically, the study found that taking soy isoflavones in doses of 60-120 mg per day improved cognitive function and visual memory in women who had gone through menopause.

When it comes to calcium, the **North American Menopause Society (2001)** points out that various bodily functions depend on it. The regulation of calcium levels in the bloodstream is a precise process that balances both excretion and absorption. The amount of calcium needed to counteract net calcium excretion remains a topic of debate. The question of the recommended intake of calcium post-menopause for Indian women to maintain bone health, as well as its role as a preventive measure against osteoporosis, is disputed. However, the guidelines of the Indian Menopause Society for 2020, based on the recommendations of the **Indian Council of Medical Research (ICMR) in 2010**, still suggest an RDA of 800 mg of calcium per day, the most current evidence available indicates.

VITAMIN E

Regarding Vitamin E, it is naturally present in a variety of foods like nuts, sunflower seeds, spinach, broccoli, and tomatoes. Hormonal imbalances during menopause can alter cortisol levels, leading to increased stress. When the body lacks antioxidants, there's a rise in free radicals that can damage cells further. Research by **Milewicz A et al. (2003)** has indicated that Vitamin E plays a role in reducing oxidative stress and aiding in the repair of cells due to its antioxidant properties. Additionally, it has been suggested that Vitamin E may alleviate symptoms of menopause such as hot flashes, regulate blood vessels, impact lipid levels in the blood, and affect changes in the vaginal area, as noted by **Ziaei, S., Kazemnejad, A., & Zareai, M. (2007)** in their study on the effect of Vitamin E on hot flashes in postmenopausal women.

REFLEXOLOGY:

Reflexology involves applying pressure techniques with the hands and fingers to specific areas on the hands and feet that are connected to every part of the body. This technique activates the body's self-healing process, providing physical relief. A clinical trial was conducted at a Gynaecology outpatient clinic with 90 menopausal women suffering from depression. The results showed that foot reflexology was effective in reducing depression symptoms during menopause, as reported by **Mahdavipour, N. M. (2019).**

HOMEOPATHY

Homeopathy is an alternative medicine approach that uses very diluted substances to stimulate the body's natural healing mechanisms. It is commonly used to treat symptoms like hot flashes, irritability, fatigue, and mood swings during menopause. Additionally, it can help with vaginal dryness and low sex drive. Women who experience hot flashes that are aggravated by heat or tight clothing may find relief with Lachesis.

ACUPUNCTURE

Acupuncture, a traditional Chinese medical practice, involves inserting tiny needles into specific body areas. It is believed to reduce pain and treat symptoms by balancing the body's energy flow. Scientific research on acupuncture has shown that it can increase endorphin levels, affecting thermoregulation in the hypothalamus and helping to manage symptoms of vasomotor syndrome.

TRADITIONAL CHINESE MEDICINE

Traditional Chinese Medicine (TCM) offers a variety of treatments for menopausal symptoms, focusing on restoring balance between Yin and Yang and supporting kidney health. TCM formulations include herbs such as colla corii asini, ginseng root, and rehmannia root, aimed at improving symptoms like dizziness, insomnia, and uterine bleeding.

A) **Black cohosh**, a plant native to North America, is a well-researched herbal remedy for menopausal symptoms. It has been found to significantly reduce overall menopausal symptoms, including hot flashes and physical discomfort, compared to a placebo. These symptoms, which affect a large number of women worldwide, can significantly impact their daily lives.

B)

Figure 1. Black cohosh

C) **St John's Wort** is primarily utilized for treating mild to moderate depression. When combined with Black Cohosh, it improves mood and lessens the severity of mood swings related to menopause.

Figure 2. St John's Wort

In a clinical trial at an academic medical center in Shiraz, Iran, 100 women participated. For eight weeks, these women were given either a placebo or an extract from St. John's wort. At two follow-up appointments, the Blatt-Kupperman Index was used to evaluate climate-related symptoms. The findings suggested that St. John's wort can effectively alleviate vasomotor symptoms in perimenopausal and postmenopausal women.

C) Evening Primerose

Oenothera biennis, also known as "evening primrose," contains a valuable oil known as EPO.

Figure: 3 Evening Primrose

A systematic review by **Yousefi et al.** indicated that evening primrose oil may reduce the severity and frequency of menopausal sweats. Similarly, **Mahboubi (2019)** and Mohammed, **Raghad et al. (2024)** conducted a systematic review that supported the use of evening primrose oil in managing menopausal vasomotor symptoms. A comparison was made between the effects of a soy oil herbal supplement and evening primrose oil on the satisfaction with treatment and quality of life in postmenopausal women. The results showed that both the soy oil supplement and evening primrose oil had a positive impact on the quality of life of postmenopausal women, although the soy oil supplement led to higher treatment satisfaction.

Postmenopausal women referred to health centers in Hamadan between May 2018 and April 2019 were part of a randomized controlled trial **by Kazemi, Farideh et al. (2021).** The intervention group consumed one capsule (1,000 mg) of evening primrose oil twice daily, while the control group received an identical quantity of placebo. The conclusion was drawn that evening primrose oil was an effective method for reducing the occurrence and intensity of night sweats.

CONCLUSION:

Menopause represents a significant biological event in the lives of women. In the field of climacteric medicine, hormone therapy for menopause remains the most common treatment method. The skill to choose the most appropriate hormone therapy for a specific individual is a crucial medical skill. This choice is backed by understanding the various clinical and metabolic effects of hormone therapy. In the last ten years, there has been a rise in the use of complementary and alternative medicine for managing menopausal symptoms, rather than hormone therapy. The ongoing refinement of clinical knowledge will enhance the therapeutic efficacy and the judicious management of patient care. Additional research endeavors are warranted concerning menopause and its associated treatment modalities.

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