

Review

Research Progress on the Treatment of Perimenopausal Syndrome in Breast Cancer Using Integrated Traditional Chinese and Western Medicine

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Abstract: With continuous improvements in the diagnosis and treatment of breast cancer, patient survival rates have significantly increased, shifting clinical attention toward enhancing quality of life during and after treatment. Endocrine therapy remains a cornerstone in the management of hormone receptor-positive breast cancer; however, the perimenopausal-like syndrome it frequently induces—characterized by hot flashes, night sweats, mood disturbances, insomnia, and joint pain—severely compromises patients' treatment adherence and overall well-being. Conventional Western medical interventions primarily rely on hormone replacement therapy and non-hormonal pharmacological agents, yet these approaches are often limited by contraindications, adverse effects, and suboptimal long-term efficacy. Traditional Chinese Medicine, with its holistic theoretical framework and individualized syndrome differentiation methodology, has demonstrated considerable potential in alleviating perimenopausal symptoms, mitigating treatment-related toxicity, and augmenting therapeutic outcomes. This review provides a comprehensive and systematic overview of recent clinical and preclinical advances in the management of perimenopausal-like syndrome in breast cancer patients using both Western and Traditional Chinese Medicine approaches. Furthermore, it critically examines the synergistic advantages, underlying mechanisms, and future prospects of integrated Traditional Chinese and Western Medicine strategies, with the ultimate aim of offering evidence-based guidance for optimizing clinical practice and improving patient-centered outcomes.

Keywords: breast cancer; perimenopausal syndrome; endocrine therapy; traditional chinese medicine; integrative medicine; quality of life

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1. Introduction

A certain type of malignant tumor ranks among the most frequently diagnosed and fatal cancers affecting women globally, posing a significant threat to female health and longevity. Advances in early detection and integrated therapeutic approaches have substantially improved five-year survival outcomes for affected individuals. For the majority of patients diagnosed with hormone receptor-positive disease, long-term postoperative endocrine modulation—typically sustained for five to ten years—serves as a fundamental strategy to mitigate recurrence risk. Commonly employed agents in this category function by either blocking estrogen signaling or suppressing its synthesis, thereby inducing a rapid decline in circulating estrogen levels. This physiological shift often precipitates a constellation of symptoms closely resembling those observed during natural perimenopause, collectively termed 'cancer-associated perimenopausal syndrome'. Conventional management options include non-hormonal pharmacological interventions and localized estrogen formulations; however, systemic hormonal supplementation is generally avoided due to theoretical concerns regarding disease

progression [1, 2]. As a result, there is growing emphasis on identifying safe, evidence-informed, non-hormonal alternatives. Traditional Chinese Medicine, with its longstanding theoretical framework centered on balancing yin and yang and alleviating perimenopausal discomfort, has seen increasing integration with contemporary clinical practice in recent years. This article provides a systematic overview of current developments from three complementary vantage points: biomedical perspectives on pathophysiology and management, Traditional Chinese Medicine conceptualizations and therapeutic approaches, and emerging directions for future investigation.

2. Definition and Treatment of Breast Cancer

According to established clinical oncology guidelines, this malignancy is currently classified into four major molecular subtypes in clinical practice: HER-2-overexpressing, triple-negative, hormone receptor-positive (HR+) Luminal A, and Luminal B. Among these, as confirmed by comprehensive cancer network guidelines and data from multiple clinical studies, hormone receptor-positive (HR+) cases represent the most common subtype worldwide, accounting for approximately 70%–80% of all diagnosed cases [3]. For patients who are positive for both the estrogen receptor (ER) and the progesterone receptor (PR), endocrine therapy has critical clinical value and serves as an important modality in postoperative adjuvant therapy and maintenance therapy following chemotherapy [4].

3. Endocrine Therapy Drugs and Perimenopausal Syndrome

3.1. Endocrine Therapy Drugs

Commonly used medications for hormone-sensitive malignancies are categorized into four groups: (1) Selective estrogen receptor modulators: The prototypical agent is tamoxifen. These agents competitively bind to estrogen receptors in tumor cells, blocking estrogen-driven proliferative signaling and thereby suppressing abnormal cellular growth; (2) Aromatase inhibitors: Anastrozole exemplifies this class. By inhibiting aromatase enzymatic activity, they impede the conversion of androgens to estrogens, resulting in reduced systemic estrogen concentrations and diminished tumor cell proliferation; (3) Ovarian function suppressants: Goserelin falls within this category. It acts on central endocrine pathways to suppress follicle-stimulating hormone and luteinizing hormone secretion, leading to decreased ovarian estrogen synthesis and release, thus restraining tumor progression; (4) Progestins: Medroxyprogesterone acetate is frequently employed [5]. It suppresses hypothalamic gonadotropin secretion, lowers follicle-stimulating hormone and luteinizing hormone production, and enhances androgen metabolism and clearance, collectively contributing to reduced overall estrogen levels [6, 7].

3.2. Perimenopausal Syndrome

The clinical manifestations of perimenopausal syndrome are complex and varied, primarily including: 1) vasomotor symptoms such as hot flashes, night sweats, and palpitations; 2) neuropsychiatric symptoms such as sleep disturbances, emotional instability, mood fluctuations, and cognitive changes; 3) urogenital symptoms such as dryness of the genital area, discomfort during intercourse, reduced sexual interest, and recurrent urinary tract infections; and 4) long-term metabolic effects including decreased bone density, joint discomfort, weight gain, and elevated cardiovascular risk. These symptoms not only significantly impair patients' daily functioning and overall well-being but also lead approximately 20%–30% of affected individuals to discontinue endocrine therapy prematurely due to symptom burden, potentially compromising treatment efficacy.

3.3. Mechanisms by Which Endocrine Therapy Drugs Induce Perimenopausal-Like Syndrome

Currently, multiple classes of endocrine-modulating agents are used clinically for adjuvant management of hormone-sensitive malignancies; their pharmacological actions

differ substantially, and the nature and intensity of treatment-induced menopausal-like symptoms vary accordingly [8, 9].

3.3.1. Selective Estrogen Receptor Modulators (SERMs; Representative Drugs: Tamoxifen, Toremifene)

Selective estrogen receptor modulators, such as tamoxifen and toremifene, function as antiestrogenic agents in certain tissues by competitively binding to estrogen receptors [10]. These agents display tissue-specific estrogenic or antiestrogenic effects in the hypothalamus, vascular system, and central nervous system. In premenopausal individuals, administration may affect the hypothalamic–pituitary–ovarian axis, resulting in elevated follicle-stimulating hormone and luteinizing hormone levels, variable ovarian estrogen production, and symptoms resembling those observed during the perimenopausal transition—including vasomotor episodes. In postmenopausal individuals, baseline estrogen concentrations are low; the modest estrogenic activity in the central nervous system is insufficient to offset systemic estrogen insufficiency, potentially contributing to thermoregulatory changes. Vasomotor symptoms occur in approximately 35% to 55% of treated individuals, a rate notably higher than that observed with aromatase inhibitor monotherapy.

3.3.2. Third-Generation Aromatase Inhibitors (AIs: Letrozole, Anastrozole, Exemestane)

Third-generation aromatase inhibitors primarily include letrozole, anastrozole, and exemestane [11]. By potently inhibiting aromatase activity, they block the conversion of androgens to estrogens in peripheral tissues such as the adrenal glands, fat, and muscle, thereby reducing serum estradiol levels in postmenopausal individuals to below 3 pmol/L, creating a state of profound estrogen deprivation far exceeding that of natural menopause. These agents lack central estrogen receptor-modulating activity; clinical adverse effects are primarily urogenital atrophy and bone and joint discomfort, with hot flashes occurring in approximately 60%–70% of cases. Prolonged estrogen deficiency may contribute to bone loss, mood changes, and metabolic alterations.

3.3.3. GnRH-a (Goserelin, Leuprolide, Ovarian Function Suppression [OFS] Regimen)

Gonadotropin-releasing hormone agonists, such as goserelin and leuprolide, are primarily used to modulate ovarian activity in premenopausal individuals with hormone receptor-positive mammary gland malignancy. Initially, these agents may transiently stimulate pituitary gonadotropin secretion; however, sustained administration leads to downregulation of luteinizing hormone and follicle-stimulating hormone release, resulting in ovarian follicular involution and a rapid decline in estrogen concentrations to postmenopausal ranges. This pharmacologically induced hypoestrogenic state accelerates the onset and intensifies the severity of treatment-induced menopausal symptoms; when administered concomitantly with aromatase inhibitors, adverse effects may be amplified [12, 13].

3.3.4. Selective Estrogen Receptor Downregulator (SERD, Fulvestrant)

As a selective estrogen receptor downregulator, fulvestrant completely antagonizes and degrades systemic estrogen receptors; it lacks tissue-selective estrogenic activity and thoroughly blocks peripheral and central estrogen signaling [14, 15]. It is commonly used for first-line and subsequent-line treatment of advanced hormone receptor-positive malignancies. Long-term use can induce a full range of estrogen-deprivation-related perimenopausal-like symptoms, with incidence rates of adverse reactions such as hot flashes and genital atrophy comparable to those observed with aromatase inhibitors.

4. Western Medical Treatment Strategies

4.1. Drug Therapy

Symptomatic drug therapy is tailored to distinct symptom clusters. Western medicine adopts a symptom-targeted approach, selecting medications to address four primary categories: vasomotor symptoms, urogenital atrophy, bone and joint pain, and psychological, emotional, and sleep-related concerns [16].

4.2. Symptomatic Medications for Vaso-Vagal Symptoms (Hot Flashes, Night Sweats)

4.2.1. Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)

Hot flashes and night sweats are the most common physical discomforts following endocrine therapy; selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors are commonly used in clinical practice. Commonly prescribed agents include paroxetine, fluoxetine, venlafaxine, and duloxetine. These medications enhance synaptic serotonin availability in the central nervous system and modulate hypothalamic thermoregulatory sensitivity, thereby reducing hot flash frequency and severity. However, potential pharmacokinetic interactions must be considered when co-administered with certain endocrine agents. Paroxetine strongly inhibits the CYP2D6 enzyme, which may impair the metabolic activation of specific hormonal therapies; thus, concurrent use requires careful evaluation and possible dosage adjustment [17]. In contrast, venlafaxine and duloxetine exhibit negligible inhibition of this enzyme pathway, supporting safer co-administration with standard endocrine regimens.

4.2.2. Central A2 Receptor Agonists

Clonidine was initially developed for blood pressure management; at low oral doses, it attenuates excessive sympathetic nervous system activity and offers modest relief from hot flashes [18, 19]. However, it commonly induces adverse effects including dry mouth, dizziness, and orthostatic hypotension, and its therapeutic effectiveness is generally lower than that of selective serotonin reuptake inhibitors and serotonin-norepinephrine reuptake inhibitors. It is typically reserved as a second-line option when first-line pharmacotherapies fail to achieve adequate symptom control.

4.2.3. Novel Neurokinin Receptor Antagonists

Neuropeptide B-mediated overactivation of KNDy neurons is the core molecular mechanism underlying hot flashes. Elinzanetant, as a dual NK1/NK3 receptor antagonist, does not affect estrogen levels and avoids stimulation of hormone-sensitive tissues; multiple Phase III clinical trials have confirmed that it rapidly and significantly improves moderate-to-severe hot flashes with good tolerability [20, 21]. It represents a breakthrough in targeted therapy for treatment-induced menopausal symptoms in recent years and holds broad application potential.

4.3. Menopausal Genitourinary Syndrome (Vaginal Dryness, Dyspareunia, Recurrent Urinary Tract Infections)

For symptoms related to genitourinary atrophy—such as dryness, pain during intercourse, and recurrent urinary tract infections—systemic estrogen therapies are generally avoided in clinical practice due to concerns about potential stimulation of previously treated hormone-sensitive tissue; low-dose localized estrogen formulations are currently preferred. Following localized administration, estradiol ointments and suppositories demonstrate minimal systemic uptake, resulting in negligible changes to circulating estrogen concentrations; long-term use has been shown to be well tolerated. These agents promote epithelial thickening, enhance glandular secretion, and help restore physiological pH balance, thereby effectively relieving discomfort associated with atrophy. Prior to initiation, coordinated evaluation by specialists in oncology and women's health is required to assess individual recurrence risk and determine appropriateness of treatment. For individuals with mild manifestations or those opting against hormonal options, non-hormonal lubricants and moisturizers may be employed. These products exhibit excellent safety profiles and support extended use as needed; however, they offer symptomatic relief only and do not address underlying structural changes. A reproductive tract-targeted selective estrogen receptor modulator has been developed specifically to improve genitourinary atrophy while avoiding activation of estrogen signaling in hormone-sensitive tissues, providing a viable alternative to localized estrogen therapy.

4.4. Medications for the Management of Aromatase Inhibitor-Associated Musculoskeletal Symptoms (Aimss)

Bone and joint pain is the most prominent adverse reaction associated with aromatase inhibitors, significantly affecting long-term treatment adherence. Supplementation with active vitamin D and calcium can alleviate joint discomfort while inhibiting excessive osteoclast activation, thereby reducing bone loss and helping prevent osteoporosis and fragility fractures; this approach constitutes a core component of supportive management [22]. Limited evidence suggests that duloxetine, low-dose prednisolone, and potassium-wasting diuretics may offer modest relief for chronic musculoskeletal pain; however, existing studies involve small sample sizes, and optimal dosing, long-term safety profiles, and precise mechanisms remain to be established through rigorous clinical investigation. For patients experiencing severe pain, nonsteroidal anti-inflammatory agents may be considered for short-term symptomatic relief, though gastrointestinal and renal risks warrant careful monitoring during extended use. Bisphosphonates and denosumab are indicated primarily for individuals with confirmed bone mineral density reduction or osteoporosis; in addition to preserving skeletal integrity, these agents may confer mild alleviation of chronic inflammatory joint symptoms.

4.5. Psychiatric Medications for Anxiety, Depression, and Insomnia

For psychological symptoms including mood disturbance, emotional dysregulation, and sleep disruption associated with endocrine therapy, clinicians prioritize anti-anxiety and antidepressant agents—such as sertraline and citalopram—that exhibit minimal inhibition of the CYP2D6 enzyme. These agents help stabilize emotional states and support psychological well-being while offering adjunctive relief for vasomotor symptoms, thus reducing the risk of pharmacokinetic interactions that could compromise antitumor treatment outcomes. Citalopram is recognized among selective serotonin reuptake inhibitors for its comparatively low CYP2D6 inhibitory activity and has been considered suitable for patients undergoing certain hormonal therapies; clinical evidence indicates no elevated risk of disease recurrence with its use. For persistent insomnia unresponsive to nonpharmacologic interventions, short-term, intermittent use of non-benzodiazepine hypnotics may be considered to mitigate dependence risks associated with conventional sedative-hypnotics.

4.6. Controversies and Restricted Use of Hormone Replacement Therapy (HRT)

Regarding hormone replacement therapy, while traditional combined systemic estrogen-progesterone treatments can comprehensively alleviate various perimenopausal symptoms, exogenous estrogen may stimulate the proliferation of estrogen receptor-positive tumor cells, substantially elevating the risk of tumor recurrence. This represents an absolute contraindication and is not routinely employed in clinical practice. Only for a very limited number of patients with severe, refractory TMS—those who have been postmenopausal for an extended period, exhibit minimal tumor recurrence risk, and remain unresponsive to multiple symptomatic pharmacologic approaches—may ultra-low-dose local hormonal application be considered following rigorous multidisciplinary evaluation, provided that therapeutic benefit demonstrably exceeds recurrence risk. Systemic oral hormonal agents must be strictly avoided throughout the entire process to safeguard antitumor treatment integrity.

4.7. Non-Pharmacological Treatments

4.7.1. Exercise Therapy

Exercise can regulate neuroendocrine levels, bone metabolism, and emotional states in the body, thereby alleviating symptoms such as hot flashes, bone and joint discomfort, insomnia, and mood-related challenges. It is also a clinically recommended rehabilitation approach for individuals undergoing endocrine therapy. Evidence indicates that regular, moderate-intensity aerobic exercise significantly improves bone and joint discomfort associated with aromatase inhibitor use. Additionally, it modulates central nervous

system neurotransmitter activity and supports emotional well-being. A clinical study is currently evaluating the effects of yoga on individuals receiving endocrine therapy, utilizing an online instruction model and employing the Functional Assessment of Cancer Therapy—Endocrine Symptoms (FACT-ES) scale as the primary outcome measure. The objective is to assess improvements in quality of life and reductions in vasomotor-related symptoms, including joint discomfort, hot flashes, and night sweats. A systematic review of exercise-based approaches during adjuvant therapy found consistent benefits across multiple domains: reduced fatigue, enhanced upper- and lower-limb muscular capacity, improved cardiopulmonary function, favorable inflammatory profiles, and better overall quality of life.

4.7.2. Psychobehavioral Interventions

Psychological and emotional symptoms are important clinical features of TIMS. The psychological stress associated with a cancer diagnosis, combined with central neurotransmitter changes linked to estrogen deficiency, contributes to increased prevalence of mood-related challenges and heightened emotional responsiveness. Currently, cognitive behavioral approaches, mindfulness-based practices, and hypnotherapy represent well-documented supportive strategies in clinical practice. Cognitive behavioral approaches have demonstrated clinically meaningful improvements in vasomotor symptoms and sleep quality among patients undergoing treatment [23, 24]. Mindfulness-based practices applied to patients experiencing mood-related challenges following endocrine therapy were associated with reductions in negative affect, enhanced present-moment awareness, and improved overall well-being. A study involving patients receiving adjuvant endocrine therapy for hormone receptor-positive malignancy found that those who received structured cognitive behavioral support reported more adaptive coping attitudes compared to controls.

4.7.3. Lifestyle Interventions

Lifestyle adjustments are characterized by low barriers to implementation and optimal safety; they primarily address systemic symptoms such as hot flashes, sleep difficulties, and weight changes [25, 26]. Hot flashes are primarily associated with fluctuations in body temperature, sympathetic nervous system activity, and elevated body weight. Evidence indicates that managing body weight, reducing intake of spicy and stimulating foods, and avoiding high-temperature environments may help reduce hot flash frequency; wearing breathable, moisture-wicking clothing can alleviate the effects of night sweats on sleep.

5. Etiology and Pathogenesis of Breast Cancer and Related Perimenopausal Syndromes

5.1. Etiology and Pathogenesis of Breast Cancer

This condition has long been recognized in traditional Chinese medicine, where it is classified under terms historically associated with mammary gland pathology; according to TCM theory, regional anatomical distinctions correspond to specific meridian pathways—the nipple region relates to the Foot Jueyin Liver Meridian, the glandular tissue to the Foot Yangming Stomach Meridian, and the surrounding area to the Foot Shaoyang Gallbladder Meridian. From a TCM perspective, pathogenesis is closely linked to functional imbalances in organs such as the liver and spleen. It is understood that disease development arises from profound depletion of the body's defensive capacity, resulting in disruption of yin-yang equilibrium and disharmony in qi and blood circulation. When the body encounters pathological influences but lacks sufficient resistance, elimination mechanisms fail, leading to stagnation of qi and stasis of blood. Prolonged stagnation promotes accumulation of damp-phlegm and internal toxin formation, which coalesce locally to form a neoplastic mass.

5.2. Etiology and Pathogenesis of Perimenopausal Syndrome Associated with Breast Cancer

Although Traditional Chinese Medicine does not recognize a condition specifically named 'perimenopausal syndrome associated with certain malignancies,' based on its clinical manifestations, it can be classified under categories such as 'various syndromes before and after menopause,' 'zangzao,' 'baihe disease,' and 'emotional constraint syndrome.' The 'Zangzao' syndrome described in the *Jingui Yaolue* closely matches the characteristics of this condition—hot flashes, insomnia, emotional fluctuations, and mental restlessness. At the same time, some scholars have observed that conditions primarily characterized by neurological and emotional manifestations align more closely with the diagnostic features of 'Baihe Disease,' a condition also first described in the *Jingui Yaolue*. The term 'Yu Syndrome' first appeared in *The Correct Transmission of Medicine*. The various physical and mental abnormalities described in the text—arising from internal injury caused by the seven emotions and stagnation of qi—closely resemble the pathological features of this condition. In 1964, 'Symptoms Before and After Menstrual Cessation' was formally incorporated into textbooks on Traditional Chinese Medicine gynecology; the physical and emotional manifestations described therein during the perimenopausal period essentially correspond to the perimenopausal syndrome recognized in modern medicine [27]. As early as the *Su Wen: Treatise on the True Nature of the Ancient Ones*, the physiological principle was proposed: 'At seventy-seven, the Conception Vessel becomes deficient, the Great Surge Vessel declines and diminishes, Tian Gui is exhausted, and the passage of the earth is blocked; therefore, the body deteriorates and one cannot bear children.' This clearly indicates that during a woman's middle age, deficiencies in the Chong and Ren meridians, the decline of Tian Gui, and imbalances in yin-yang, qi, and blood can induce a series of physical and psychological discomforts. This classical theory also became the core pathogenic mechanism underlying the later concept of 'various symptoms before and after the cessation of menstruation.' The *Su Wen: On the True Nature of the Ancient Times* outlines the physiological characteristics of women in middle age, namely the gradual decline of essence and blood and the gradual depletion of *tian gui*. However, in patients with certain malignancies, surgery and chemotherapy deplete qi and blood, compounded by the long-term depleting effects of endocrine medications. This leads to deficiency of liver and kidney yin essence and the generation of internal deficiency heat, which in turn triggers a series of yin deficiency manifestations, including hot flashes, night sweats, insomnia, fatigue, malnourishment of tendons and bones, and dryness of the reproductive tract. At the same time, due to the impact of the tumor and long-term medication, patients experience emotional distress and stagnation of liver qi. This stagnation transforms into excess heat, which affects mental clarity and sleep quality, exacerbating emotional and sleep-related manifestations. Prolonged impairment of qi circulation affects the spleen and stomach, giving rise to phlegm-turbidity and blood stasis. These pathogenic factors intertwine to obstruct the Chong and Ren meridians, further aggravating symptoms such as generalized discomfort and menstrual irregularities. Overall, this condition is characterized by yin deficiency of the liver and kidneys and an imbalance of the Chong and Ren meridians. Emotional constraint triggers various pathological changes involving phlegm, blood stasis, and heat. These factors intertwine to form a self-perpetuating pattern, leading to recurrent and protracted symptoms. Clinical treatment must address both the root cause and the manifestations: by tonifying the liver and kidneys and harmonizing the Chong and Ren meridians to consolidate the foundation, and by soothing the liver, regulating emotions, transforming phlegm, and resolving blood stasis to manage the manifestations, thereby restoring the body's yin-yang balance.

6. Traditional Chinese Medicine Treatment for Perimenopausal-Like Syndrome Associated with Breast Cancer

Traditional Chinese Medicine (TCM) adopts a personalized, syndrome-differentiation-based approach to managing perimenopausal-like symptoms following endocrine therapy for hormone-sensitive malignancies [9]. Conventional TCM interventions include herbal decoctions, acupuncture, gua sha, and therapeutic massage.

6.1. Internal Treatment Methods in Traditional Chinese Medicine

Internal treatment in TCM primarily involves the oral administration of herbal decoctions [28]. Following the principles of syndrome differentiation and treatment, this approach holistically regulates the qi, blood, and yin-yang of the zang-fu organs, alleviating various physical and emotional symptoms. It does not interfere with hormonal levels or antagonize the efficacy of endocrine therapy, making it exceptionally safe.

Research exploring internal treatment methods from the perspectives of "deficiency, stagnation, and heat" has applied modified Erzhi Pills or Chaihu Jia Longgu Muli Decoction for initial management. Patients reported notable improvement in symptoms including numbness in the extremities, subjective sensations of internal warmth, sweating, and disrupted sleep characterized by shallow depth and early morning awakening. For subsequent management, Chaihu Jia Longgu Muli Decoction combined with Huangqi Guizhi Wuwu Decoction—appropriately modified—was administered; after a two-month follow-up, patients experienced no significant discomfort. Another study applied Chaihu Jia Longgu Muli Decoction together with Shen Siwei Huacai Decoction for perimenopausal-like syndrome associated with endocrine therapy, observing marked improvements in vasomotor symptoms such as hot flashes and sweating, as well as mood-related manifestations including low mood and restlessness attributed to deficient yang rising. The overall response rate in the intervention group reached 73.33%. Statistically significant reductions were observed in both the Greene Menopause Scale and TCM syndrome scores, while Karnofsky Performance Status (KPS) scores improved ($P < 0.05$). A proprietary formula termed "Nourish Earth, Nourish Water, and Calm the Spirit Decoction", developed based on principles of tonifying the kidneys and strengthening the spleen, and nourishing yin while subduing yang, demonstrated effectiveness in improving vasomotor instability, psychoneurological symptoms, and dermatological manifestations. A randomized controlled trial involving 55 participants with aromatase inhibitor-associated perimenopausal-like syndrome found that the group receiving modified Chaihu Jia Longgu Muli Decoction achieved significantly better outcomes on the modified Kupperman Index and TCM syndrome scores compared to controls ($P < 0.05$), with notable relief of hot flashes, sweating, insomnia, and irritability. Clinical practice guided by the principle of soothing the liver, strengthening the spleen, and tonifying the kidneys identified "stagnant heat in the liver meridian" as the predominant pattern through data mining. Treatment emphasized clearing liver heat, resolving constrained qi flow, cooling the blood, and regulating physiological cycles [29]. Frequently used herbs included those targeting liver qi regulation and heat-clearing, blood-cooling actions. This strategy aimed to mitigate adverse effects of endocrine therapy while supporting ongoing anticancer management. Further clinical investigation identified Liver Qi Stagnation and Kidney Essence Deficiency as core pathomechanisms, leading to the application of a Liver-Regulating, Poria- and Polygonatum-Based Menstrual Regulation Decoction. Results indicated significant reduction in the Kupperman Symptom Index, improvement in quality-of-life assessments, and favorable modulation of hormonal profiles, T-cell subsets, and lipid metabolism.

6.2. External Treatment Methods in Traditional Chinese Medicine

External therapies in Traditional Chinese Medicine (TCM) are non-pharmacological, "green" therapeutic approaches. Based on meridian-based pattern differentiation, they utilize external stimulation to harmonize the zang-fu organs, promote the flow of qi and blood, and balance yin and yang. These therapies can effectively alleviate various physical and emotional symptoms of TIMS without affecting patients' hormonal levels or the efficacy of anticancer treatment [30, 31]. Suitable for long-term rehabilitation applications, they have become an important component of TCM approaches for TIMS.

Relevant clinical observations have revealed that when patients experiencing perimenopausal-like discomfort following endocrine therapy for mammary carcinoma were treated with auricular acupoint patch therapy, the overall symptom scores in the observation group decreased significantly, and levels of hormones and lipid-related

indicators also improved markedly. The differences between groups were statistically significant ($P < 0.05$), confirming the practical clinical value of auricular acupoint patch therapy in managing this type of complication [2, 17]. Furthermore, existing studies have confirmed that acupuncture can regulate the secretion levels of gonadotropin-releasing hormone (GnRH) in the hypothalamus, thereby explaining at the central nervous system level the underlying mechanism by which acupuncture alleviates hot flashes secondary to endocrine therapy for mammary carcinoma. At the same time, acupuncture therapy can also positively regulate the functions of endocrine glands such as the pituitary gland and exert regulatory effects on various immune components, including complement, cytokines, and phagocytes. By leveraging systemic nonspecific regulatory effects, it improves the body's overall condition and alleviates various physical discomforts experienced by patients. A study specifically targeted patients with perimenopausal syndrome classified as "yin deficiency with internal heat" according to pattern differentiation during endocrine therapy for mammary carcinoma, investigating the clinical efficacy and safety of Li's copper scraper gua sha combined with oral Chinese herbal medicine. The study enrolled 60 female participants diagnosed with mammary carcinoma who were undergoing endocrine therapy and met the criteria for the corresponding pattern. Participants were randomly assigned to two groups, each with a sample size of 30. The control group received only the oral formula Chaihu Shugan San combined with Liuwei Dihuang Tang with appropriate modifications, while the treatment group received the same oral herbal protocol supplemented with external Li-style copper scraper gua sha therapy. A comparison of the efficacy data between the two groups showed that the overall response rate in the treatment group reached 96.7%, which was significantly higher than that of the control group ($P < 0.05$). After completion of the therapeutic protocol, patients in the treatment group scored higher than those in the control group on measures of physical, social, emotional, and role functioning, as well as overall health status, while reporting lower scores for discomfort symptoms such as fatigue, insomnia, chest tightness and shortness of breath, and constipation. Research has found that acupuncture combined with auricular seed implantation can effectively alleviate core symptoms such as hot flashes, sweating, insomnia, and palpitations. Significant clinical results have been achieved in treating this condition by combining Liuwei Dihuang Wan with the "Baduanjin" exercise protocol. Clinical observation has shown that acupuncture at the Yinxi and Fulu acupoints effectively alleviated sweating associated with the "heart-kidney disharmony" pattern following endocrine therapy for premenopausal mammary carcinoma, and also improved patients' emotional distress and low mood. A systematic meta-analysis was conducted on the use of TCM external therapies for treating perimenopausal-like syndrome following endocrine therapy for mammary carcinoma. The results showed that, compared with endocrine therapy alone, the combination of TCM external therapies (acupuncture, auricular acupuncture, medicated plasters, etc.) demonstrated significant advantages in improving the clinical response rate, Kupperman score, TCM syndrome score, and symptoms of hot flashes and sweating.

6.3. Combination of Internal and External Therapies

The integrated treatment of internal and external methods in TCM is rooted in the philosophy of "combining internal and external factors for holistic treatment." The *Ling Shu* states, "Internal factors refer to internal injuries to the zang-fu organs, while external factors correspond to the meridians on the body surface," clearly indicating that imbalances in the qi and blood of the zang-fu organs can manifest externally on the meridians and body surface, while stimulation of the meridians on the body surface can also internally regulate the yin and yang of the zang-fu organs. The pathological location of this condition lies in the liver, kidneys, and the Chong and Ren meridians. Internally, deficiency of the liver and kidneys, failure of yin to restrain excess heat, and stagnation of qi constitute the fundamental pathogenesis, while externally, hot flashes, insomnia, pain, and emotional instability represent the manifest symptoms. Internal administration of

Chinese herbal medicine, formulated based on pattern differentiation, tonifies the liver and kidneys, nourishes yin and clears excess heat, soothes the liver and alleviates emotional tension, and transforms phlegm and resolves blood stasis [26]. This approach addresses the root cause by regulating imbalances in the qi, blood, and yin-yang of the zang-fu organs and improving endocrine function within the body; External therapies such as acupuncture, acupoint plaster application, and ear acupoint seed therapy stimulate meridians and acupoints to unblock the flow of qi throughout the body, harmonize qi and blood, and calm the mind and stabilize mental equilibrium, thereby rapidly alleviating various physical and emotional manifestations. Internal treatments address the root cause, while external treatments address the manifestations; the synergy between internal and external approaches enables bidirectional modulation, aligning with the complex pathogenesis of this condition—characterized by a combination of deficiency at the root and excess at the branch, as well as a mixture of deficiency and excess—resulting in more comprehensive, lasting, and stable therapeutic outcomes compared to monotherapy. Clinical trials have confirmed the overall efficacy of combining acupuncture with oral administration of the "Tiaohe Decoction" in managing perimenopausal syndrome associated with endocrine therapy following oncological treatment. This combined approach demonstrated greater advantages than either the Tiaohe Decoction or venlafaxine used independently; it significantly alleviated various physical discomforts and improved patients' quality of life without causing fluctuations in estrogen levels. While effectively managing perimenopausal-like symptoms, it maintained compatibility with the original anticancer endocrine therapy. Oral administration of Danggui Shaoyao San combined with external application of Chinese herbal acupoint patches has yielded favorable clinical outcomes in patients experiencing perimenopausal syndrome after oncological surgery and subsequent endocrine therapy. A randomized controlled study enrolled 90 participants, assigning them equally to a combined acupuncture and herbal medicine group, a herbal medicine-only group, and an acupuncture-only group; post-treatment assessment showed that improvement in the modified Kupperman score was significantly greater in the combined group than in the other two groups, with statistically significant intergroup differences ($P < 0.05$). Animal experiments further indicated that the combined acupuncture and herbal medicine approach could restore ovarian physiological function in perimenopausal model rats, promote endometrial proliferation and thickening, and increase peripheral blood estradiol levels. Collectively, these findings indicate that, compared to oral Chinese herbal medicine alone or acupuncture alone, the combined acupuncture and herbal medicine approach offers more pronounced comprehensive benefits. It not only rapidly alleviates diverse clinical manifestations but also favorably modulates endogenous estrogen secretion.

7. Summary and Outlook

Currently, Western medicine offers limited treatment options for perimenopausal syndrome in patients undergoing oncological care, primarily relying on symptomatic management; moreover, some agents used to alleviate symptoms may interfere with endocrine-modulating therapies. Grounded in the holistic principle of pattern differentiation and treatment, Traditional Chinese Medicine (TCM) interprets the underlying pathophysiology and commonly applies interventions including oral herbal formulations, acupuncture, moxibustion, and acupoint application, demonstrating notable clinical benefits. However, a standardized, consensus-based framework for pattern differentiation remains underdeveloped. Future efforts should integrate systems biology and network pharmacology approaches to clarify the mechanisms of herbal formulae, establish consistent criteria for pattern classification and outcome assessment, implement multicenter clinical investigations, and formulate evidence-informed, scalable diagnostic and therapeutic protocols—thereby advancing synergistic integration of TCM and Western medical approaches in this domain.

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