ORIGINAL RESEARCH ARTICLE

Effects of kuntai capsule in combination with hormone replacement therapy on premature ovarian failure and bone metabolism

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*Aidong Shen[1],Yajun Ren[1],Jing Ling[2],Junxu Zhou[2] and Yangyan Sun[2]**

Center for Bone Joint, Jiangyin Clinical College, Xuzhou Medical University, Jiangsu Province, China[1]; Department of Gynecology, Jiangyin Clinical College, Xuzhou Medical University, Jiangsu Province, China[2]

***For Correspondence:** Email: *luanfan9713@163.com*; Phone: 13812157297

Abstract

This study evaluates the clinical effectiveness of combining kuntai capsule with hormone replacement therapy (HRT) in treating premature ovarian failure (POF) and its impact on ovarian reserve and bone metabolism. A total of 190 POF patients were randomly assigned to either a control group (n=95) receiving HRT alone (1 mg estradiol valerate tablets and 10 mg dydrogesterone tablets), or an observation group (n=95) receiving a combination of HRT and Kuntai Capsule. After three months of treatment, the observation group showed significantly better ovarian reserve, with a higher overall effective rate (87.37% vs. 71.58%). Hormonal analysis revealed lower follicle-stimulating hormone (FSH) and luteinizing hormone (LH) levels, and higher estradiol (E2) levels in the observation group compared to the control. Furthermore, ovarian reserve markers such as anti-Müllerian hormone (AMH) and antral follicle count were also higher in the observation group. Bone metabolism improvements were noted, with higher osteocalcin (OST) and lower bone-specific alkaline phosphatase (BAP) levels. The observation group also had a significantly lower recurrence rate (7.3%) after 24 months, compared to the control group (16.8%). These results suggest that the combination of Kuntai Capsule and HRT offers a promising treatment for POF, improving ovarian function, hormone levels, and bone health while reducing recurrence risk. *(Afr J Reprod Health 2025; 29 [5]: 63-73).*

Keywords: Kuntai Capsule; HRT; POF; Bone metabolism

Résumé

Cette étude évalue l'efficacité clinique de l'association de la capsule Kuntai à un traitement hormonal substitutif (THS) dans le traitement de l'insuffisance ovarienne prématurée (IOP) et son impact sur la réserve ovarienne et le métabolisme osseux. Au total, 190 patientes atteintes d'IOP ont été randomisées soit dans un groupe témoin (n = 95) recevant un THS seul (comprimés de valérate d'estradiol à 1 mg et de dydrogestérone à 10 mg), soit dans un groupe d'observation (n = 95) recevant une association de THS et de la capsule Kuntai. Après trois mois de traitement, le groupe d'observation présentait une réserve ovarienne significativement meilleure, avec un taux d'efficacité global plus élevé (87,37 % contre 71,58 %). L'analyse hormonale a révélé des taux d'hormone folliculo-stimulante (FSH) et d'hormone lutéinisante (LH) plus faibles, ainsi que des taux d'estradiol (E2) plus élevés dans le groupe d'observation que dans le groupe témoin. De plus, les marqueurs de la réserve ovarienne, tels que l'hormone anti-müllérienne (AMH) et le nombre de follicules antraux, étaient également plus élevés dans le groupe témoin. Des améliorations du métabolisme osseux ont été observées, avec des taux d'ostéocalcine (OST) plus élevés et des taux de phosphatase alcaline osseuse (PAO) plus faibles. Le groupe témoin présentait également un taux de récidive significativement plus faible (7,3 %) après 24 mois, par rapport au groupe témoin (16,8 %). Ces résultats suggèrent que l'association de la capsule Kuntai et du THS constitue un traitement prometteur de l'IOP, améliorant la fonction ovarienne, les taux hormonaux et la santé osseuse, tout en réduisant le risque de récidive. *(Afr J Reprod Health 2025; 29 [5]: 63-73).*

Mots-clés: Capsule Kuntai ; THS ; IOP ; Métabolisme osseux

Introduction

Premature ovarian failure (POF) describes the diminished ovarian function among women under the age of 40, resulting from various factors. Approximately 1% of women younger than 40 and 5% of women under the age of 45 experience spontaneous POF[1]. Estrogen, produced by the ovaries, is one of the crucial hormones influencing bone metabolism. It primarily promotes osteoblast activity and inhibits osteoclast activity, thereby maintaining bone calcium content and bone mineral density (BMD)[2]. Furthermore, estrogen facilitates intestinal calcium absorption and renal calcium

reabsorption, thus increasing the total calcium level in the body. When estrogen levels decline, bone metabolism becomes imbalanced, leading to an increased risk of osteoporosis[3]. In cases of POF, the significant drop in estrogen levels results in reduced calcium absorption and retention, further exacerbating bone metabolic imbalance and the risk of osteoporosis[4]. Multiple cross-sectional studies have shown that the BMD of patients with POF is reduced compared to control groups[5].

Another study has established that early menopause is linked to a heightened risk of fractures in old age[6]. Recently, a prospective observational investigation further confirmed that women who undergo menopause prior to the age of 47 face a greater risk of developing osteoporosis and sustaining fractures later on, compared to the control group[7].

Hormone replacement therapy (HRT), which establishes an artificial menstrual cycle through exogenous hormone supplementation, is a crucial measure for treating menopausal symptoms, preventing bone loss, and promoting cardiovascular health in patients with POF[8]. HRT for POF offers significant benefits, including the alleviation of low estrogen symptoms, prevention of osteoporosis, and improvement of cardiovascular health. However, it does not fundamentally cure the disease[9]. Kuntai Capsule is a Traditional Chinese medicine (TCM) formulation comprising six herbal ingredients: Rehmannia Glutinosa, White Peony Root, Poria, Colla Corii Asini, Coptis Chinensis, and Scutellaria Baicalensis[10]. Kuntai Capsule can promote follicular development and alleviate symptoms caused by POF, such as insomnia, night sweats, hot flashes, facial flushing, soreness and weakness of the waist and knees, etc[11-13].

A meta-analysis has shown that the concomitant use of Kuntai Capsule can significantly boost estrogen (E2) levels in patients with POF[14]. The combination of Kuntai Capsule with hormone therapy seems to decrease the level of follicle-stimulating hormone (FSH), enhance the number of antral follicles in the ovary and elevate serum anti-Müllerian hormone (AMH) extent in diminished ovarian reserve (DOR) patients[15]. Furthermore, in the management of polycystic ovary syndrome (PCOS) patients, combination of letrozole (LE) with Kuntai Capsule exhibits superior efficacy compared to LE alone, largely attributed to its capacity to boost ovarian function and modulate sex hormone levels in the body[16]. These studies collectively confirm that Kuntai Capsule can enhance ovarian function and regulate sex hormone levels.

A randomized controlled trial was conducted, involving the combination of 12 different types of TCM with HRT. The results indicated that patients receiving HRT combined with these 12 oral TCMs had a higher overall clinical response rate compared to those receiving HRT alone[17]. Despite the promising preliminary results suggesting the efficacy of combining TCM with HRT, there is a lack of confirmation from large-sample clinical trials for specific TCM formulations like Kuntai Capsule. This study addresses this gap by conducting a rigorous, large-scale clinical trial to investigate the advantages of this particular combined treatment regimen. By doing so, we aim to provide robust evidence to support the use of Kuntai Capsule in conjunction with HRT as a viable and potentially more effective treatment option for POF. Furthermore, our study seeks to contribute to the body of knowledge on the integrative approach to managing POF, which combines the strengths of both conventional Western medicine (HRT) and TCM. This integrative approach may offer a more holistic and personalized treatment option for patients with POF.

Methods

Participants

One hundred and ninety patients diagnosed with POF who sought treatment at the Jiangyin People's Hospital between January 2020 and July 2022 were enrolled. The diagnostic criteria to the standards for POF outlined in "Obstetrics and Gynecology"[18]. The diagnosis of POF was established by two measurements of follicle-stimulating hormone (FSH) levels exceeding 30IU/L, taken at intervals of more than 4 weeks apart. The patients were randomly assigned to either the control or the observation group (95 cases in each group).

The inclusion criteria were: 1) patients who met the diagnostic criteria for POF; 2) all individuals were 18 years or older; and 3) those who signed informed consent forms. The exclusion criteria were: 1) women with concomitant uncontrolled heart failure, respiratory failure, liver cirrhosis, hepatitis, chronic kidney disease, etc.; 2) those with hematologic diseases such as leukemia; 3) women with

concomitant immune system diseases such as systemic lupus erythematosus, rheumatoid arthritis, etc.; 4) those with malignant tumors, schizophrenia, depression, etc.; desire to become pregnant; and 5) those using sex hormone medications within the past 3 months. Participants were advised to avoid taking herbal medicines or calcium supplements during the study period. Women who were taking medications that could potentially affect bone density or had diseases known to impact bone density were excluded.

Treatment

The control group underwent hormone replacement therapy, administered in accordance with the menstrual cycle. Treatment commenced on the 5th day of the initial menstrual cycle, with patients taking 1 mg of Estradiol Valerate Tablets once daily for 21 days. Beginning on the 16th day of the first menstrual cycle, patients were also prescribed 10 mg of Dydrogesterone Tablets twice daily for 10 consecutive days, ceasing both medications simultaneously. This treatment regimen was maintained for a total of three menstrual cycles. Bedsides the standard treatment protocol administered to the control patients, the observation group was also given Kuntai Capsules (produced by Guiyang Xintian Pharmaceutical Co., Ltd.). The dosage for Kuntai Capsules was 4 capsules per dose, taken three times daily, orally administered 30 minutes after meals, for a continuous period of 30 days. A three-month period constituted one full course of treatment for the observation group.

Hormone levels

Venous blood was collected from all patients before treatment and after three menstrual cycles of treatment. The serum was separated to measure hormone levels, including Follicle-Stimulating Hormone (FSH), Luteinizing Hormone (LH), and Estradiol (E2) using FSH ELISA kit (Elabscience, Wuhan, China), LH ELISA kit (Elabscience) and E2 ELISA kit (Elabscience), respectively.

Ovarian reserve function

Venous blood samples were obtained from patients pretherapy and post-treatment to measure the level of serum Anti-Müllerian Hormone (AMH) using corresponding enzyme-linked immunosorbent assay (ELISA) kit (Beyotime Biotechnology, Shanghai, China). Additionally, vaginal B-ultrasound examinations were conducted to monitor the number of antral follicles.

Bone metabolism

Venous blood samples were obtained from all patients prior to the initiation of treatment and following three menstrual cycles of treatment. The serum was separated to measure the levels of bone metabolism indices, including Osteocalcin (OST) and Bone-specific Alkaline Phosphatase (BAP) using corresponding ELISA kits.

Clinical efficacy

The clinical efficacy was assessed using a tiered evaluation system that categorized patients into three groups[18]: marked effectiveness (normalization of sex hormone levels, resumption of menstruation with regular cycle length and volume for >3 months), effectiveness (improvement in sex hormone levels, resumption of menstruation but with a prolonged cycle and decreased volume for >3 months), and ineffectiveness (failure to achieve the aforementioned criteria). The overall effective rate was calculated by taking the total of cases showing marked effectiveness and effectiveness, dividing it by the total number of cases, and then multiplying the result by 100%.

Statistical methods

Statistical analysis is conducted using GraphPad Prism 10 software. Quantitative results areexpressed as Mean ± SD ($\bar{x} \pm s$). For comparisons between two groups, independent sample t-tests were employed, whereas paired t-tests were utilized for within-group comparisons. Comparisons between groups were conducted using χ^2 tests. Statistical significance was defined as a P-value<0.05.

Ethical consideration

This research was approved by the Institutional Review Board (IRB) from Jiangyin People's Hospital, which operates in compliance with the relevant ethical guidelines and regulations. All participants in this study provided informed written consent prior to their involvement. The research

team has adhered to the highest standards of ethical conduct throughout the study, including maintaining confidentiality of participant information, ensuring that the risks to participants are minimized, and providing appropriate compensation or incentives for their participation

Results

Baseline characteristics in the two groups

Two hundred and twenty four (224) women were initially screened. However, 34 women were excluded because their FSH level was below 30 IU/L. Consequently, 190 females were enrolled in the study. Recruitment was terminated due to time constraints, 190 patients were randomly allocated to the observation group and the control treatment group, each comprising 95 patients. The control group included patients aged 27 to 44 years, with a mean age of 38.52 ± 3.87. The participants' BMI values ranged between 21.3 and 24.5 kg/m², with a mean of 22.92 ± 0.75 kg/m². The duration of their illness spanned from 6 to 15 months, with a mean duration of (9.41±3.22) months. The observation group included patients aged between 32 and 44 years, with a mean age of 39.78±2.97. The participants' BMI values ranged from 21.5 to 29.1 kg/m², with a mean of 24.9 ± 1.58 kg/m². The duration of their illness varied from 5 to 16 months, with a mean duration of 9.67 ± 3.75 months. There were no statistically significant differences in the baseline characteristics between the two patient groups. The research process is illustrated in Figure 1.

Clinical efficacy in two groups

The observation group achieved 52 cases of marked effectiveness, 31 effective cases, and 12 ineffective cases, resulting in an overall effective rate of 87.37%. The control group had 46 cases of marked effectiveness, 22 effective cases, and 27 ineffective cases, yielding an overall effective rate of 71.58%. Significantly, the observation group exhibited an elevated overall effective level compared to the control group.

Comparison of hormone levels

Prior to treatment, the patients in the observation group exhibited FSH, LH, and estradiol (E2) levels of (53.62±6.48) mIU/L, (35.18±4.32) mIU/L, and (24.52±4.73) ng/L at 24 months, respectively. At 24- months post-treatment, these levels shifted to (31.27±4.19) mIU/L, (26.52±3.78) mIU/L, and (53.19±6.38) ng/L, respectively. In contrast, the control group's pre-treatment levels of FSH, LH, and E2 were (54.27±6.31) mIU/L, (36.82±4.51) mIU/L, and (23.86±4.21) ng/L, respectively, which adjusted to (36.58±5.22) mIU/L, (20.64±3.21) mIU/L, and (44.42±6.11) ng/L at 24- months post-treatment. Significantly, post-treatment hormone levels revealed that the observation had lower levels of FSH (P<0.05, Figure 2A) and LH (P<0.05, Figure 2B) compared to the control, whereas the E2 level (P<0.05, Figure 2C) was higher in the observation group. These differences were statistically significant.

Ovarian reserve function indicators

Before therapy, the observation group exhibited serum AMH levels of (0.91±0.42) ng/mL and a count of antral follicles of (0.98±0.12). At 24-months post-treatment, these values changed to (6.62±0.79) ng/mL and (2.24±0.23), respectively. In the control, the pre-treatment levels of serum AMH and the number of antral follicles were (0.88±0.12) ng/mL and (0.94±0.32), respectively, which shifted to (3.76±0.58) ng/mL and (1.67±0.43) at 24- months post-treatment. After clinical therapy, the females in the observation queue demonstrated significantly higher abundance of AMH (P<0.05, Figure 3A) and a larger number of antral follicles (P<0.05, Figure 3B) when compared to the corresponding control queue.

Comparison of bone metabolism indicators

Prior to treatment, the observation queue had serum levels of OST and BAP of 20.19 ± 4.54 ug/L and 113.36 ± 16.51 U/L, respectively. Following treatment, these levels changed to 30.43 ± 4.15 ug/L and 84.35 ± 10.72 U/L at 24- months post-treatment. In contrast, the control group's pre-treatment levels of OST and BAP were 20.48 ± 4.07 ug/L and 114.73 ± 15.82 U/L, which shifted to 26.75 ± 5.23 ug/L and 101.45 ± 12.17 U/L at 24- months post-treatment. Notably, the observation group exhibited remarkedly higher OST levels and lower levels of BAP compared to the control queue at 24-months post-treatment (P<0.05, Figure 4).

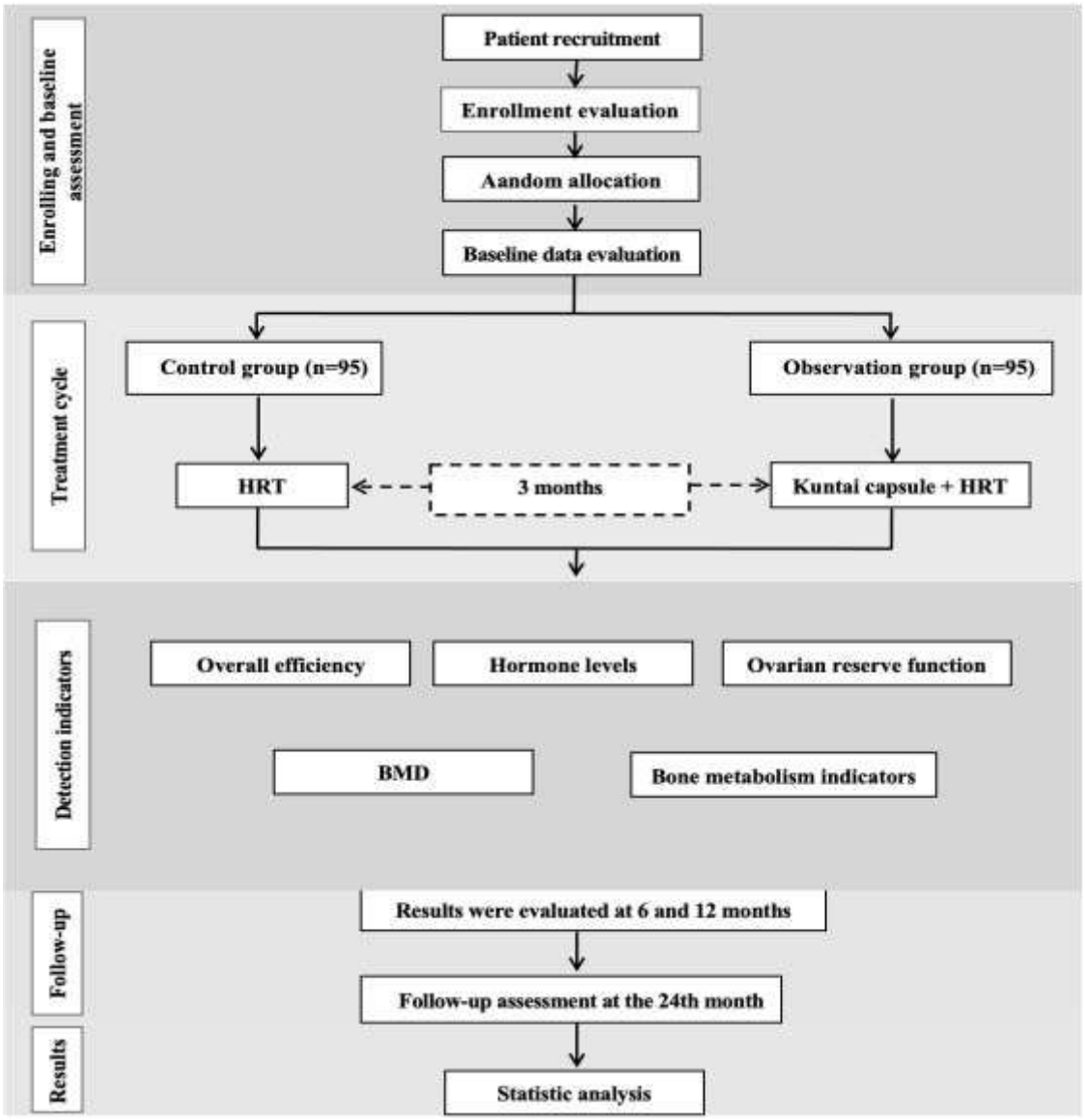

Figure 1: Presents a flowchart that illustrates the research procedure

Table 1: The effective level in the two sets [n(%)]

Group	Number of cases	Marked effective	Effective	Ineffective	Overall effective rate (%)
Control	95	46	22	27	71.58
Observation	95	52	31	12	87.37
χ^2 value					5.803
***P*-value**					0.016

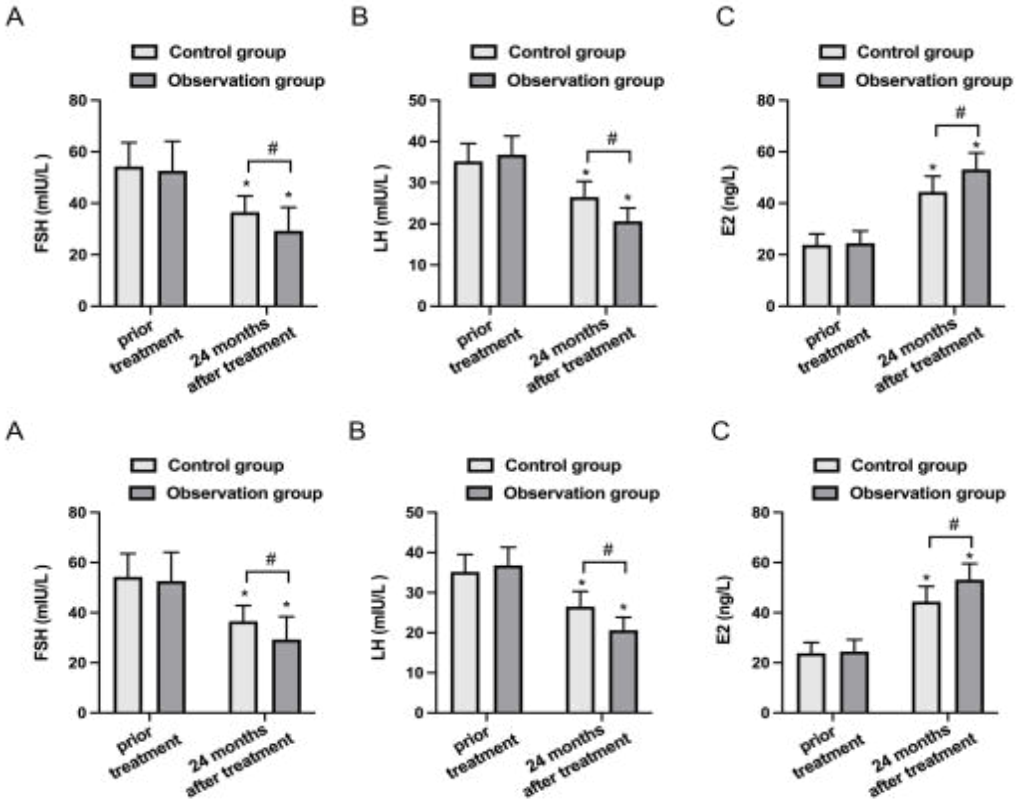

Figure 2: Comparison of hormone levels pre- and post-treatment between the two patient groups. (A) FSH levels, (B) LH levels, and (C) E2 levels. Compared to pretherapy, $^{*}P<0.05$. In comparison to the control, $^{\#}P<0.05$

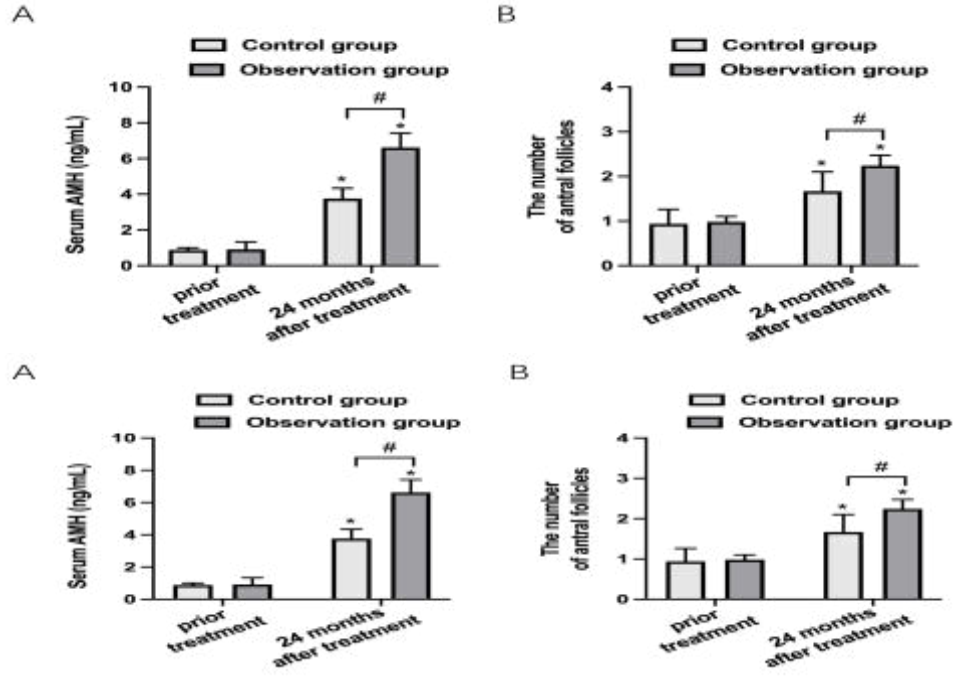

Figure 3: Comparison of the antral follicle count and serum AMH level pretherapy and post-treatment. (A) Serum AMH levels, (B) Antral follicle count. Compared to pre-treatment levels, $^{*}P<0.05$. Compared to the control, $^{\#}P<0.05$.

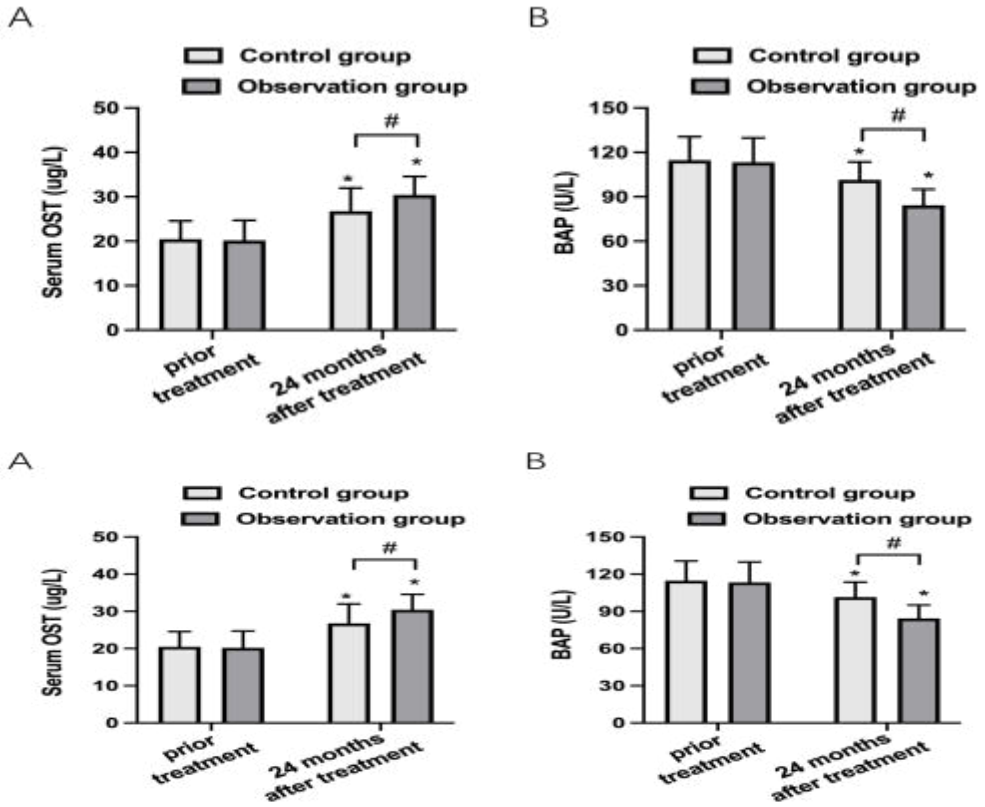

Figure 4: Comparison of OST and BAP levels pretherapy and post-treatment. (A) Serum OST levels, (B) Serum BAP levels. Compared to pre-treatment levels, $^{*}P<0.05$. Compared to the control queue, $^{\#}P<0.05$.

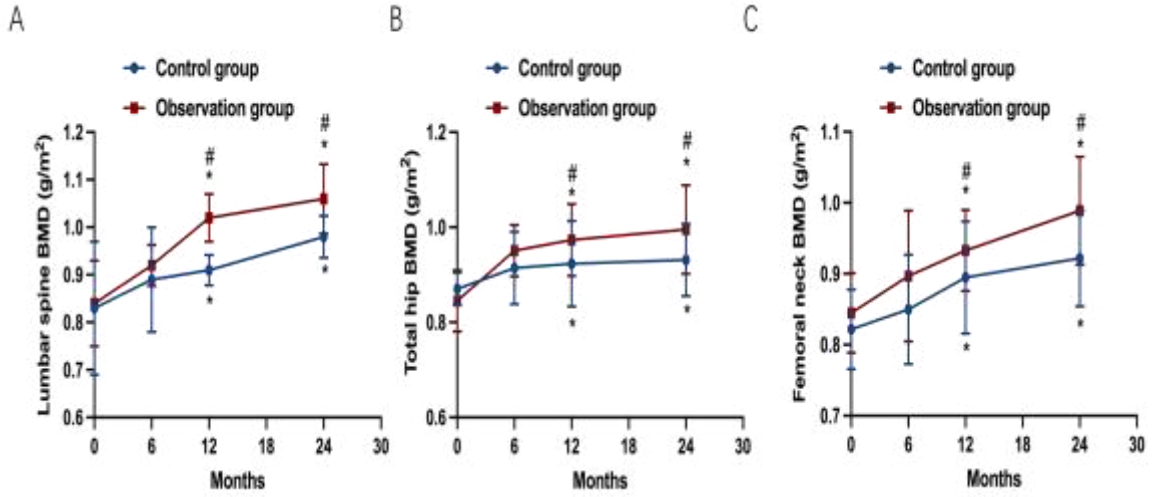

Figure 5: Comparative analysis of bone mineral density (BMD) in the lumbar spine, hip joint, and femoral neck between the two groups. (A) Lumbar spine BMD (g/m²), (B) Hip BMD (g/m²), and (C) Femoral neck BMD (g/m²) in pretherapy and post-treatment. Compared to the pretherapy levels, $^{*}P<0.05$. Compared to the control queue, $^{\#}P<0.05$.

Comparison of BMD of the lumbar spine, hip joint, and femoral neck between the two groups

6- months post-treatment, no significant difference was observed in the lumbar spine BMD between the observation and control groups. At 12- and 24- months post-treatment, both the observation and control groups exhibited remarkedly increases in lumbar spine BMD compared to pre-treatment (P<0.05, Figure 5A). The patients from the observation group displayed a more pronounced increase in lumbar spine BMD compared to the patients from the control group at 12-months post-treatment (1.02 ± 0.05 g/m^2 *vs*. 0.91 ± 0.03 g/m^2, P<0.05, Figure 5A). At 24- months post-treatment, the increase in the lumbar spine BMD was remarkedly greater in the observation queue than in the control queue (1.06 ± 0.07 g/m^2 *vs*. 0.98 ± 0.04 g/m^2, P<0.05, Figure 5A). At 6- months post-treatment, no significant difference was observed in the total hip BMD between the observation and control groups. Both groups also demonstrated increases in the total hip BMD at 12 and 24 months, with a more significant elevation at 24 months (P<0.05, Figure 5B). At 12- months post-treatment, the increase in the total hip BMD was remarkedly greater in the observation queue than in the control queue (0.973 ± 0.076 g/m^2 *vs*. 0.923 ± 0.09 g/m^2, P<0.05, Figure 5B). At 24- months post-treatment, the increase in the total hip BMD was remarkedly greater in the observation queue than in the control queue (0.995 ± 0.093 g/m^2 *vs*. 0.931 ± 0.076 g/m^2, P<0.05, Figure 5B). At 6- months post-treatment, no significant difference was observed in the femoral neck BMD between the observation and control groups. Additionally, at 12- months post-treatment, the observation group maintained a significantly higher femoral neck BMD than the control group (0.933 ± 0.057 g/m^2 *vs*. 0.895 ± 0.079 g/m^2, P<0.05, Figure 5C). At 24- months post-treatment, the observation group maintained a significantly higher femoral neck BMD than the control group (0. 989 ± 0.076 g/m^2 *vs*. 0.922 ± 0.068 g/m^2, P<0.05, Figure 5C).

The recurrence rate in the two treatment groups

After completing treatment, patients were monitored for 24 months to evaluate recurrence, defined as meeting the diagnostic criteria for POF. During this follow-up period, there were 18 recurrent cases in the control group, resulting in a recurrence rate of 16.8% (18 out of 107 patients). On the contrary, the observation queue had 6 recurrent cases, leading to a recurrence rate of 7.3% (6 out of 82 patients, χ^2 = 4.01, P<0.05).

Discussion

POF is a gynaecological endocrine disorder, primarily manifested by persistent menopause and genital atrophy, along with elevated gonadotropin levels and decreased estrogen levels[19]. Among Chinese women, the incidence of POF ranges between 1% and 4%, and it has shown an increasing trend in recent years, particularly affecting younger women, thereby significantly impacting their reproductive health and overall quality of life[20]. Modern medical theories suggest that the onset and progression of POF are linked to multiple factors, including genetics, immune mechanisms, abnormalities in gonadotropins and their receptors, among others[21]. The primary approach in Western medicine for treating POF is HRT, which effectively enhances ovarian follicle function and alleviates the symptoms and signs associated with low estrogen levels. POF is characterized by a decrease in estrogen levels, and estrogen is vital for bone metabolism. Specifically, estrogen promotes calcium absorption and bone formation, while inhibiting bone resorption and the activity of osteoclasts. When premature ovarian failure occurs, the reduction in estrogen levels leads to an imbalance in bone metabolism, which in turn can trigger bone problems such as osteoporosis.

The core principle of HRT lies in mimicking the natural fluctuations in hormone levels that occur during a woman's regular menstrual cycle[22]. This therapy primarily involves a sequential administration of estrogen and progesterone, which has been proven effective in inhibiting the secretion of FSH and enhancing the ovaries' sensitivity to it[23]. This, consequently, has a critical impact on enhancing ovarian function and overall reproductive health. Additionally, HRT exerts a profound beneficial effect on the hypothalamic-pituitary-gonadal axis, precisely regulating the levels of LH. An increase in LH levels not only addresses the issue of low estrogen levels in the body but also facilitates the restoration of a regular

menstrual cycle[24]. By doing so, HRT contributes to a more balanced hormonal environment, promoting overall well-being and quality of life for women undergoing this treatment. HRT has certain efficacy in treating premature ovarian failure, but it also has some limitations, such as limited therapeutic effects[25]. HRT is primarily used to alleviate symptoms caused by ovarian function decline, such as menopausal symptoms and osteoporosis, but its ability to restore ovarian function is limited[26]. It cannot reverse the process of premature ovarian failure or fully restore normal ovarian function. Furthermore, each patient's response and treatment outcome vary. Some patients may experience symptom improvement with HRT, but this does not necessarily mean that ovarian function has been substantially restored[27].

While HRT can replenish the estrogen deficiency in the body, thus alleviating bone metabolism disorders to some degree, the risk of osteoporosis associated with prolonged premature ovarian failure remains[28]. HRT is not capable of fully reversing established osteoporosis. Certain patients may observe an increase in bone density following HRT administration, whereas others may witness only minimal enhancement. The abnormalities in bone metabolism resulting from premature ovarian failure may stem from additional factors[29]. Consequently, depending solely on HRT may not yield optimal therapeutic outcomes. Patients should also incorporate other therapeutic approaches to holistically address bone metabolism disorders. Therefore, it is necessary to seek more effective treatments to improve premature ovarian failure.

Kuntai Capsule is based on the Huanglian Ejiao Tang recipe documented in the "Shanghan Lun", and it possesses the efficacy of nourishing yin and blood, tonifying the kidneys, and benefiting the marrow[30]. In this formulation, Shu Di Huang (Rehmanniae Radix Praeparata) is the key ingredient, while Bai Shao (Paeoniae Radix Alba), Huang Lian (Coptidis Rhizoma), and E Jiao (Colla Corii Asini) serve as supporting ingredients. Fu Ling (Poria) and Huang Qin (Scutellariae Radix) act as assistant ingredients[31,32]. Collectively, the formula works to warm and nourish the liver and kidneys, replenish essence and marrow, nourish yin and blood, calm the mind, tranquilize the spirit, and harmonize yin and yang. Kuntai Capsules are a proprietary Chinese medicine that is widely used in the treatment of menopause and related postmenopausal disorders[31,33]. This medication has demonstrated efficacy in improving uterine artery blood flow, regulating menstruation, mitigating related symptoms, and modulating endocrine function in individuals with reduced ovarian reserve[3]. Liu *et al*. disclosed that the therapeutic benefits of Kuntai Capsules in primary ovarian insufficiency are primarily mediated through the regulation of multiple signaling pathways, including tumor necrosis factor (TNF), forkhead box O (FOXO1) , mitogen-activated protein kinase (MAPK), and phosphoinositide-3-kinase/serine/threonine kinase 1 (PI3K/AKT)[13]. However, there is currently no published research examining the potential effectiveness of combining Kuntai Capsule with HRT for the management of POF.

The observed differences in hormone levels between the two groups provide further insight into the mechanisms underlying the efficacy of the combination therapy. The observation group exhibited lower levels of FSH and LH, as well as higher levels of E2 compared to the control group. These alterations in hormone levels in line with the restoration of ovarian function and the alleviation of POF symptoms. Furthermore, the observation group exhibited enhancements in ovarian reserve function indicators, characterized by increased serum levels of AMH and a higher count of antral follicles. AMH is a well-recognized indicator of ovarian reserve, and its elevation in the observation group implies a beneficial effect on ovarian function. The rise in the number of antral follicles provides additional support for the idea that the combination therapy may stimulate ovarian follicle growth and enhance fertility prospects. In addition to its effects on ovarian function, the combination therapy also had a positive impact on bone metabolism. The females in the observation group showed higher OST levels and lower BAP levels compared to the control group. These changes are indicative of improved bone health and reduced risk of osteoporosis, which is a common complication in patients with POF due to estrogen deficiency.

In conclusion, the combination of Kuntai Capsule and HRT demonstrates promising clinical results in the treatment of POF. It effectively alleviates symptoms, restores hormone balance, enhances ovarian function, improves bone metabolism, and reduces the risk of disease recurrence. These findings suggest that Kuntai Capsule may be a

valuable addition to the therapeutic arsenal for the management of POF, offering a potential alternative or adjunct to traditional HRT. Further explorations are needed to elaborate the mechanisms of action of Kuntai Capsule and to confirm its long-term safety and efficacy in larger patient populations.

Strengths and limitations

This study on combining Kuntai Capsule with HRT for POF has several strengths, including a randomized controlled design, large sample size, and significant findings. However, it also has limitations, such as the lack of blinding and potential confounding factors. The implications of the results for policy and practice include updates to treatment guidelines, further research, improved patient care, and public awareness.

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Conflict of interests

The authors declare no competing interests.

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Author contributions

A.D.Shen: Designed the study, supervised the research, and contributed to manuscript writing.Y.J. Ren: Conducted the data analysis and helped in manuscript drafting.J.Ling: Assisted with the experimental design and provided insights on the clinical implications of the study.J.X.Zhou: Managed patient recruitment, clinical data collection, and performed data interpretation.Y.Y.Sun: Led the research team, contributed to the study design, and critically revised the manuscript for intellectual content.

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