Assignment 2

ISci 701

Maryland University of Integrative Health

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Summary of Results

Finished Herbal Product as an Alternative Treatment for Menopausal Symptoms in Climacteric Women was a twelve week study conducted in Taiwan. The aim of the study was to evaluate the efficacy of herbal medicines in treating menopausal women. To do so, the study was an observational study of patients from four hospitals in Taiwan. The authors of the study used specific inclusion and exclusion criteria and provided the intervention is a standard and organized fashion, carefully measuring changes.

This study is no different than most of the available literature on herbal protocols. The study wasn't conducted following all of the same guidelines that we would like to see in a well designed study, however the results are still clinically useful. While the study did not compare to a control group, there was some statistical difference in hot flashes and other symptoms amongst the women, chiefly between those with mild symptoms and those with moderate to severe symptoms. This study would not lead me to conclusively determine that the TMN-1 finished herbal product would be a panacea for menopausal symptoms, however it would make me want to conduct further research and potentially recommend the treatment to women with few other options with better supporting documentation.

Effects of Kuntai Capsule and hormone replacement therapy on cognitive function and mental symptoms of early postmenopausal women: a randomized controlled trial, was carried out in China, comparing hormone replacement therapy to a Chinese medicine, Kuntai plant capsule. The study was specifically evaluating the interventions for effectiveness in treating cognitive and mental symptoms related to menopausal symptoms in Chinese women. Various tests were used to measure effectiveness and look for adverse reactions to the treatments. The results of the study did not show a statically significant difference between the two treatment groups.

The study is applicable to the population that I am likely to interface with, insofar as it refers to women who are, will be, or have gone through menopause and experienced related symptoms. One major downfall of this study is that it is limited to women from one particular area of China and would not be an accurate representation of the racial diversity in the group that I would interface with. The study is most applicable in that it shows promise in an alternative to hormone replacement therapy that should be further studied, using a larger sample size.

References:

Lai, J., Hwang, J., Chen, H., & Wang, J. (2005). Finished Herbal Product as an Alternative Treatment for Menopausal Symptoms in Climacteric Women. *The Journal of Alternative and Complementary Medicine,11*(6), 1075-1084. doi:10.1089/acm.2005.11.1075

Li, W. (2010). Effects of Kuntai Capsule and hormone replacement therapy on cognitive function and mental symptoms of early postmenopausal women: a randomized controlled trial. *Journal of Chinese Integrative Medicine,8*(4), 321-327. doi:10.3736/jcim20100404

Methodology Checklist 2: Controlled Trials

SIGN

Study identification (*Include author, title, year of publication, journal title, pages*)

Lai, J., Hwang, J., Chen, H., & Wang, J., Finished Herbal Product as an Alternative Treatment for Menopausal Symptoms in Climacteric Women, 2005 THE JOURNAL OF ALTERNATIVE AND COMPLEMENTARY MEDICINE Volume 11, Number 6, pp. 1075–10845

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

SECTION 1: INTERNAL VALIDITY

	In a well conducted RCT study…	***Does this study do it?***
1.1	The study addresses an appropriate and clearly focused question. The study addressed the safety and efficacy of a specific herbal product for the treatment of menopausal symptoms in a specific population.	Yes ☐X No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised. This study did not compare interventions or have a control group. All participants were given the same herbal intervention, meaning that there were no separate treatment groups.	Yes ☐ No ☐X Can't say ☐
1.3	An adequate concealment method is used. Does not apply given information in 1.2	Yes ☐ No X☐ Can't say ☐
1.4	The design keeps subjects and investigators 'blind' about treatment allocation. Does not apply in this study since all participants received the same intervention.	Yes ☐ No X Can't say ☐
1.5	The treatment and control groups are similar at the start of the trial. All participants received the same intervention so there was no control group.	Yes ☐ No X Can't say □
1.6	The only difference between groups is the treatment under investigation. The groups were divided by location of clinical site, not by intervention.	Yes ☐ No ☐X Can't say ☐
1.7	All relevant outcomes are measured in a standard, valid and reliable way. The Kupperman Index (KI) was used as the primary outcome measure for this study. As a secondary measure, form WHOQOL-BREF was used. This is hard to assess without further training. Intuition tells me that these forms and measurements	Yes ☐ No ☐ Can't say X

	would produce subjective results given that they rely on study participants to self-report.	
1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? 18% of the study participants dropped out of the 12 week study.	18%
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis). Given lack of randomization, this does not apply.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐X
1.10	Where the study is carried out at more than one site, results are comparable for all sites. This study was carried out at 4 different sites with similar results.	Yes X No ☐ Can't say ☐ Does not apply ☐

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise bias? *Code as follows:* I would say that this study minimized bias in that it used acceptable inclusion and exclusion criteria for study participants and utilized standard measurements for outcome assessments. The study did not include the allocation concealment or blinding that would be expected of an a well executed clinical trial.	High quality (++)☐ Acceptable (+)☐X Low quality (-)☐ Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

Methodology Checklist 2: Controlled Trials

Study identification (*Include author, title, year of publication, journal title, pages*)

Li, W, A Randomized Controlled Clinical Study on the Effects of Kuntai Capsule and Hormone Replacement Therapy on Cognitive Function and Mental State of Early Postmenopausal Women, Journal of Integrated Traditional Chinese and Western Medicine: Volume 8 April, 2010 Number 4

Guideline topic:	Key Question No:	Reviewer:

Before completing this checklist, consider:

1. Is the paper a **randomised controlled trial** or a **controlled clinical trial**? If in doubt, check the study design algorithm available from SIGN and make sure you have the correct checklist. If it is a **controlled clinical trial** questions 1.2, 1.3, and 1.4 are not relevant, and the study cannot be rated higher than 1+
2. Is the paper relevant to key question? Analyse using PICO (Patient or Population Intervention Comparison Outcome). IF NO REJECT (give reason below). IF YES complete the checklist.

Reason for rejection: 1. Paper not relevant to key question ☐ 2. Other reason ☐ (please specify):

SECTION 1: INTERNAL VALIDITY

In a well conducted RCT study…		***Does this study do it?***
1.1	The study addresses an appropriate and clearly focused question. The question involved a specific population (40 - 60 year old postmenopausal women from a particular hospital) and two very specific interventions being compared (estrogen hormone replacement therapy and Kuntai capsule).	Yes ☐x No ☐ Can't say ☐
1.2	The assignment of subjects to treatment groups is randomised. The study used computer block randomization.	Yes ☐x No ☐ Can't say ☐
1.3	An adequate concealment method is used. This was not mentioned in the study.	Yes ☐ No ☐ Can't say ☐x
1.4	The design keeps subjects and investigators 'blind' about treatment allocation. This was also not mentioned in the study, only that the women were randomly assigned to groups.	Yes ☐ No ☐ Can't say ☐X
1.5	The treatment and control groups are similar at the start of the trial. Yes, the algorithm split the women into groups of 29 and 28, respectively.	Yes X☐ No ☐ Can't say ☐
1.6	The only difference between groups is the treatment under investigation. The same inclusion and exclusion criteria was applied to all study participants. Differences in size and weight were compared with no significant difference.	Yes ☐X No ☐ Can't say ☐
1.7	All relevant outcomes are measured in a standard, valid and reliable way. Measurements were taken in a way that could be repeated and would be reliable. The study used biochemical analysis and MMSE, Kupperman index and QOL scores at several different junctures.	Yes ☐X No ☐ Can't say ☐

1.8	What percentage of the individuals or clusters recruited into each treatment arm of the study dropped out before the study was completed? The group taking the CEE hormone replacement therapy had a 14% drop out rate over the course of 12 months. The group taking the Kuntai therapy had a 21% drop out rate.	CEE/HRT Group - 14% of the group dropped out Kuntai - 21%
1.9	All the subjects are analysed in the groups to which they were randomly allocated (often referred to as intention to treat analysis). Specifically mentions Intention to treat analysis.	Yes ☐X No ☐ Can't say ☐ Does not apply ☐
1.10	Where the study is carried out at more than one site, results are comparable for all sites.	Yes ☐ No ☐ Can't say ☐ Does not apply ☐X

SECTION 2: OVERALL ASSESSMENT OF THE STUDY		
2.1	How well was the study done to minimise bias? *Code as follows:* This study could be considered acceptable since a computer algorithm was used to randomly assign the study participants to treatment groups, however I have to rate it low quality. Without explicit mention of blinding or allocation concealment, it is hard to know if bias was adequately minimized.	High quality (++)☐ Acceptable (+)☐ Low quality (-) X Unacceptable – reject 0 ☐
2.2	Taking into account clinical considerations, your evaluation of the methodology used, and the statistical power of the study, are you certain that the overall effect is due to the study intervention?	
2.3	Are the results of this study directly applicable to the patient group targeted by this guideline?	
2.4	**Notes.** Summarise the authors' conclusions. Add any comments on your own assessment of the study, and the extent to which it answers your question and mention any areas of uncertainty raised above.	

[Effects of Kuntai Capsule and hormone replacement therapy on cognitive function and mental symptoms of early postmenopausal women: a randomized controlled trial].

Clinical treatises

Journal of Integrated Traditional Chinese and Western Medicine: Volume 8 April, 2010 Number 4

DOI: 10.3736 / jcim20100404

A Randomized Controlled Clinical Study on the Effects of Kuntai Capsule and Hormone Replacement Therapy on Cognitive Function and Mental State of Early Postmenopausal Women

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BACKGROUND: Combination of estrogen (conjugated equine estrogen, CEE) is one of the commonly used drugs for hormone replacement therapy and is limited in perimenopausal and postmenopausal women due to safety problems. For patients with hormone replacement therapy contraindications and caution patients, traditional Chinese medicine treatment to become another choice.

OBJECTIVE: To compare the effects of Chinese medicine Kuntai capsule and CEE on cognitive function and psychological status of early menopausal women and to evaluate their safety.

Design, site, object and intervention measures: 57 cases of early postmenopausal outpatients in Huaxi Women and Children's Hospital of Sichuan University were randomly divided into two groups: the Kuntai group (28 cases) and the hormone group (29 cases). The patients were treated and observed for 1 year. Kuntai Kuntai capsule administered group (each 0.5 G), 2 G / time, 3 times / D ; the hormone group received CEE 0.6 mg / d and 0.3 mg / d alternately (mean 0.45 mg / D), there uterus , Plus medroxyprogesterone acetate, 2 mg / d .

The main outcome indicators: from the date of every 3 months to evaluate a cognitive function and mental state, record adverse reactions to intentional analysis (intention to treat, ITT) and per-protocol set (PPS).

Results: The cognitive function, Kupperman index and quality of life (QOL) scale of the Mini Mental State Examination (MMSE) were analyzed at the time points after treatment. (P <0.05), but there was no significant difference between the hormone group and the Kuntai group after treatment (P > 0.05) , but there was no significant difference between the two groups (P > 0.05). The MMSE scores of two groups showed a gradual increase trend, Kupperman index and QOL psychological symptom score showed a gradual decline trend. (39.3%) was higher than that of Kuntai group (11.1%), and the difference was statistically significant ($\chi^2 = 5.750$, $P = 0$), but there was no significant difference between the two groups (P <0.05). 029), the remaining adverse reactions, the difference between the two groups were not statistically significant. **Conclusion:** Kuntai Capsule and CEE have a certain effect on maintaining normal cognitive function and improving psychological symptoms in early postmenopausal women.

Li WJ, LZ Xu, Liu HW, Zhang J, Tang, LL, LL Zhou, Zhuang J, Liu the Y, Liu XF *J lntegr Chin Med* 2010;. 8 (. 4):. Received November 12 is 321-327, 2009; accepted. March 1, 2010; published online April 15, 2010. Indexed / abstracted in and full text link-out at PubMed. Journal title in PubMed: *Zhong Xi Yi Jie He Xue Bao* . Free full text (HTML and PDF) is available at http : //www.jcimjournal.com . Forward linking and reference linking via CrossRef. DOI: 10.3736 / jcim20100404

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Women in the perimenopausal and postmenopausal changes in hormone levels, there can be a series of physical, mental symptoms and mild cognitive impairment (MCI). MCI is often seen as an early manifestation of dementia, the most common dementia is Alzheimer's disease (AD). (11.48%) was higher than that of men (7.05%) in the elderly population aged over 70 years in the United States . [1] The prevalence of female AD was higher than that of men (7.05%) . In our elderly women, the prevalence of AD is 9.58% to 10.89%, women have a higher risk than men [2] .

Brain as an important target organ of estrogen, leading memory and cognitive function, animal and in vitro cell studies have shown that estrogen has a protective effect on brain structure. Combined with estrogen (conjugated equine estrogen, CEE) is one of the commonly used drugs for hormone replacement therapy, but because of safety problems, its use in perimenopausal and postmenopausal women are limited. For patients with hormone replacement therapy contraindications and caution patients, traditional Chinese medicine treatment to become another choice. Kuntai Capsule (formerly known as New Year's Nourishing Capsule) is a listed non-prescription compound Chinese medicine preparation, mainly used for the treatment of premenopausal disorders. To compare the efficacy and safety of kuntai capsules and estrogen in cognitive function and psychological symptoms of early menopausal women, we conducted a one-year, prospective, randomized, controlled, parallel group of clinical trials.

1 Materials and Methods

1.1 Clinical data

1.1.1 subjects in September 2005 ~ October 2006, to raise and screen Sichuan University of China Women and Children Hospital outpatient treatment of 40 to 60 years of postmenopausal women as the subjects.

1.1.2 included in the standard (1) uterine, menopause ≥ 3 months and ≤ 3 years, no uterine, hysterectomy ≤ 3 years; (2) with hot flashes, sweating, depression, mood swings and other menopausal related symptoms (3) Serum estradiol (E2) ≤ 30 ng / L, follicle-stimulating hormone (FSH) ≥40 IU / L (subjects with bilateral ovariectomy excluded) This standard); (4) no estrogen-dependent malignancy, no severe liver and kidney dysfunction and other hormone replacement therapy contraindications.

1.1.3 exclusion criteria (1) currently suffering from uterine fibroids, fibroids ≥ 3 cm, endometriosis with obvious signs and symptoms; diagnosis of diabetes and hypertension history, a history of thromboembolic disease or thrombosis The formation of tendencies; epilepsy, asthma, hyperprolactinemia, first-degree relatives of breast cancer family history. (2) physical illnesses that are in serious or unstable conditions, including liver, kidney, gastrointestinal tract, cardiovascular, respiratory, endocrine, neurological, immune or hematologic diseases. (3) previous three months of alcohol or drug abuse or dependence history. (4) within nearly a month has been taking estrogen preparations or menopause-related symptoms of health care products. (5) withdrawal of the drug after the endometrial thickness ≥ 0.5 cm, cervical cytology showed abnormalities other than inflammation. (6) unexplained postmenopausal vaginal bleeding. (7) previous test drug (CEE, medroxyprogesterone acetate, kuntai capsules) allergy. (8) had participated in a clinical trial of another study drug within 30 days prior to the study of the first interview.

1.2 Research Methods

1.2. 1 Study packet after screening 57 eligible subjects were divided into groups and hormones in the screening of group Kuntai computer block randomization method, wherein the hormone 29 cases, 28 cases Kuntai.

1.2. 1 Study packet after screening 57 eligible subjects were divided into groups and hormones in the screening of group Kuntai computer block randomization method, wherein the hormone 29 cases, 28 cases Kuntai.

1.2.2 Treatment regimen Hormone group (CEE, 0.3 mg / pellet, Wyeth Pharmaceutical Co., Ltd., supplied by Beijing Pharmaceutical Company, production lot number 0404154, valid until October 2008), CEE 0.6 mg / d and 0.3 mg / d Alternative use (average 0.45 mg / d), oral, uterine plus medroxyprogesterone acetate (Zhejiang Xianju medicine, 2 mg / tablets, provided by Sichuan University, West China Second Hospital), 2 mg / d; Thai Group (Kuntai Capsule, Guiyang Xintian Pharmaceutical Co., Ltd., 0.5 g / grain, approved the number of Zhunzi Z20000083, the production batch number is 20050202, valid until November 2008), 4 / time, 3 Times / d Two groups of continuous treatment of drugs for 12 months.

1.2.3 Observations

1.2.3.1 Cognitive function and mental state assessment The mental state-related items in the Mini-Mental State Examination (MMSE), Kupperman Menopause Index and Menopausal Quality of Life Scale were used. The subjects were investigated before, 3, 6, 9 and 12 months after treatment, including orientation, memory, attention, ability to calculate, recollection, language ability, presentation ability and drawing ability. , And add the total score. Dementia severity grading method: mild MMSE ≥ 21 points; moderate MMSE ≥ 10 points, ≤ 20 points; severe MMSE ≤ 9 points. The Kupperman Mental Symptom Score includes patients with subjective depression, suspicion, mood swings, insomnia scores, each of which is multiplied by a factor of 0, 1, 2, 3, The Postmenopausal quality of life mental illness items include memory loss, anxiety, depression, depression, lack of patience, reluctance to contact the crowd and mental state of the evaluation.

1.2.3. 2 general condition age, ethnicity, height, body weight, waist circumference, hip circumference, natural or artificial menopause age, body system physical examination.

1.2.3.3 hormone test using chemiluminescence method before and after treatment of fasting blood insulin and before treatment E2, FSH levels (Siemens ADVIA Centaur chemiluminescence instrument and supporting reagents).

1.2.3.4 blood biochemical examination before and after treatment using Hitachi Hitachi 7600 automatic biochemical analyzer and supporting reagents were detected liver and kidney function, blood lipids, fasting blood glucose, the detection method for the turbidimetric method.

1.2.3.5 Adverse reactions All subjects were issued diary card, record the amount of vaginal bleeding and breast pain during the test period, and before and after treatment to do breast mammography, pelvic ultrasound and ECG examination. All occurrences are recorded with or without adverse events, the time of occurrence of the event, the severity of the incident, the relationship with the test drug (unrelated, unlikely, may be relevant, likely to be relevant, most likely about 5 grades) Incident measures taken.

1.3 Medical ethics This study has been approved by the Beijing Municipal Union Medical College Ethics Committee. All subjects were informed of the nature of the study and signed informed consent.

1.4 statistical methods measured using ` $x \pm s$ description, the test method using two samples t test, skewed distribution data using the median and quartile spacing description and Kruskal-Wallis test; count data using chi-square test. Kupperman index, postmenopausal quality of life score score in the psychological status index and MMSE score using repeated measurement of variance analysis. According to intention-to-treat, ITT) and the per-protocol set (PPS) principle. ITT analysis, that is, all randomized subjects, whether or not they were included in the analysis, were included in the analysis, and the missing follow-up results were treated according to the recent observation of the carry-over principle; PPS analysis, ie, randomization was included in the inclusion criteria, Of the major variables were completed and the subjects who completed the entire trial were analyzed. P <0.05 for the difference was statistically significant. All analyzes using SPSS 13.0 software.

2 Results

2.1 General conditions Screening period in line with the inclusion criteria, and received randomized group of postmenopausal women in a total of 57 cases. ITT analysis of hormone group included 29 cases, Kuntai group included 28 cases. 24 cases of hormone group were consistent with PPS analysis, 19 cases of Kuntai group in line with PPS analysis. The test flow chart shown in Figure 1 , the subjects at all times to complete the follow-up situation in Table 1

FIG 1 randomized trial flowchart of

Figure 1 Flow diagram of this randomized trial

Table 1 Number of follow-up of the two groups at each time point were completed

Table 1 Patients completed follow-up at each time point in two groups

Group	*N*	Number of patients			
		3 months	6 months	9 months	12 months
CEE	29	28	24	23	25
Kuntai	28	25	21	20	22

2.2 Baseline characteristics Kuntai group and hormone group general population data in addition to waist to hip ratio, the remaining difference was not statistically significant (see Table 2). Including uterine in 51 cases, no uterine in 6 cases. Hormone group, the screening of hepatitis B combined . 1 Example gallstones 2 Example lumbar cracked . 1 Example allergic asthma . 1 Example lumbar disc . 1 Example antral polyp . 1 cases; Kuntai group, cholecystitis screening Merged . 1 Example gallstones . 1 cases of appendicitis . 1 Example lumbar disc . 3 cases of chronic gastritis 2 cases, right bundle branch block . 1 Example cervical disc . 1 Example cervical osteoarthritis . 1 cases of genital herpes . 1 Example Double breast resection in 1 case, breast milk hyperplasia in 1 case.

Table 2 Two sets of baseline characteristics

Table 2 Characteristics of baseline data in two groups

Items	CEE group	Kuntai group	*P* value
Age (` *x* ± *s* , years)	49.21 ± 4.08	48.89 ± 4.21	0.78
Age at menopause (` *x* ± *s* , years)	47.48 ± 3.85	47.25 ± 4.21	0.83
Menopausal time (Median, months)	18.0	11.5	0.38
Body mass index (kg / m2)	21.86 ± 2.39	21.07 ± 1.70	0.16
Waist-hip ratio (` *x* ± *s*)	0.89 ± 0.05	0.86 ± 0.06	0.02
E2 (` *x* ± *s* , ng / L)	14.66 ± 8.22	13.36 ± 8.02	0.55
FSH (` *x* ± *s* , IU / L)	77.54 ± 20.72	78.74 ± 18.17	0.82
Systolic blood pressure (` *x* ± *s* , mmHg)	112.64 ± 10.36	114.64 ± 12.63	0.66
Diastolic blood pressure (` *x* ± *s* , mmHg)	74.64 ± 8.42	73.14 ± 8.48	0.55

The MMSE score showed a trend of increasing with the time of treatment (ITT analysis $P = 0.02$, PPS analysis $P = 0.045$). Compared with the Kuntai group, the MMSE scores of the two groups were different No statistical significance (ITT analysis $P = 0.24$, PPS analysis $P = 0.353$, see Table 3). In the case of ITT analysis, the MMSE score (27.89 ± 3.99) decreased after 3 months of treatment (ITT analysis decreased 0.32 points), but did not meet the clinical significance (see Figure 2). Groups Kupperman mental state score decreases each time point (with prolonged treatment ITT analysis P <from 0.001 , the PPS Analysis P <0. 001), the hormone group and the Kuntai group, the difference was not statistically significant (ITT analysis $P = 0.614$, PPS analysis $P = 0.394$). The two groups at each time point quality of life scores showed a gradual downward trend (ITT analysis P<0.001 , PPS analysis P <0.001); comparing the hormone group and Kuntai group, the difference was not statistically significant (ITT analysis $P = 0.117$, PPS analysis $P = 0.334$). See Table 3 . 001 , PPS analysis P <0.001). There was no significant difference between the hormone group and the Kuntai group (ITT analysis $P = 0.117$, PPS analysis $P = 0.334$). See Table 3 . 001 , PPS analysis P <0.001). There was no significant difference between the hormone group and the Kuntai group (ITT analysis $P = 0.117$, PPS analysis $P = 0.334$). See Table 3 .

Table 3 two groups at each time point MMSE and psychological status score of ITT and PPS analysis
Table 3 ITT and PPS analyses of cognitive and mental changes in MMSE, Kupperman index and quality of life at each time point in two groups

($\bar{X} \pm s$)

Data set	Group	*N*	MMSE	Kupperman index	Quality of life
ITT	CEE				
	Before treatment	29	27.97 ± 2.78	4.90 ± 3.02	12.66 ± 8.14
	Three-month treatment	29	28.76 ± 2.18 *	3.37 ± 2.74 **	7.83 ± 8.99 **
	Six-month treatment	29	29.17 ± 2.09 *	3.03 ± 2.50 **	7.31 ± 6.42 **
	Nine-month treatment	29	29.17 ± 2.11 *	2.72 ± 2.99 **	5.97 ± 6.26 **
	Twelve-month treatment	29	29.28 ± 2.07 *	2.34 ± 2.44 **	4.83 ± 7.33 **
	Kuntai				
	Before treatment	28	28.21 ± 3.84	5.68 ± 3.49	12.96 ± 11.01
	Three-month treatment	28	27.96 ± 4.02 *	3.46 ± 2.78 **	10.46 ± 10.02 **
	Six-month treatment	28	28.61 ± 3.10 *	3.61 ± 3.86 **	8.25 ± 10.56 **
	Nine-month treatment	28	28.96 ± 2.20 *	2.54 ± 2.56 **	5.04 ± 6.22 **

	Twelve-month treatment	28	28.89 ± 2.20 *	2.14 ± 2.49 **	5.46 ± 6.54 **
PPS	CEE				
	Before treatment	twenty four	27.25 ± 6.11	4.67 ± 3.12	13.38 ± 8.74
	Three-month treatment	twenty four	29.29 ± 1.20 *	3.17 ± 2.71 **	8.25 ± 9.83 **
	Six-month treatment	twenty four	29.79 ± 0.59 *	2.63 ± 2.18 **	7.29 ± 6.80 **
	Nine-month treatment	twenty four	29.79 ± 0.66 *	2.25 ± 2.74 **	5.46 ± 6.45 **
	Twelve-month treatment	twenty four	29.92 ± 0.28 *	2.00 ± 2.23 **	4.38 ± 7.72 **
	Kuntai				
	Before treatment	19	28.95 ± 1.47	5.32 ± 3.68	13.21 ± 12.47
	Three-month treatment	19	29.00 ± 1.92 *	2.95 ± 2.91 **	8.32 ± 7.90 **
	Six-month treatment	19	29.79 ± 0.54 *	3.42 ± 4.48 **	7.47 ± 11.87 **
	Nine-month treatment	19	29.95 ± 0.23 *	1.79 ± 2.64 **	2.79 ± 4.33 **
	Twelve-month treatment	19	29.79 ± 0.54 *	1.47 ± 2.46 **	3.26 ± 4.82 **

* $P < 0.05$, ** $P < 0.01$, *vs* before treatment.

Figure 2 groups at each time point MMSE score of ITT and PPS analysis

Figure 2 ITT and PPS analyses of MMSE scores at each time point in two groups

2.4 Safety indicators

2.4.1 Blood biochemical tests ITT and PPS analysis showed that the two groups of high-density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride (triglyceride, TG), BUN (Blood urea nitrogen, BUN), creatinine (creatinine, of Cr), and serum alanine aminotransferase (alanine aminotransferase, the ALT) has decreased compared with before treatment, TG before treatment liters ($P > 0.05$). The levels of LDL , ALT and BUN in the hormone group were lower than those before treatment ($P <0.05$). ITT analysis showed that fasting insulin and fasting blood glucose before and after treatment were no significant changes ($P > 0. 05$), LDL was significantly lower than before treatment ($P <0.05$). PPS analysis showed that fasting blood glucose hormone therapy group was significantly higher than that before (Treatment $P <0.05$), but were within the normal range (990.25 ± 50.42) mg / L .

2.4.2 other laboratory tests before and after breast mammography, ECG and cervical cytology were found no clinical significance of the abnormal. Pelvic B ultrasound showed a single layer of endometrial thickness were <0.5 cm .

2.5 Adverse reactions A total of 55 patients who were followed up at once were included in the adverse reaction evaluation. There were 28 cases of hormone group , 19 cases of adverse events , 27 cases of Kuntai group , 17 cases of adverse events , the difference between the two groups, the difference was not statistically significant ($\chi2 = 0.146$, $P = 0. 781$). Wherein the hormone group and the group Kuntai most common adverse reactions are breast tenderness (Kuntai group 14 patients hormone group 13 is cases), the incidence of vaginal bleeding in the hormone group (39.3%) after breast tenderness, Kun Thailand group was 11.1% , the difference between the two groups, the difference was statistically significant ($\chi2 = 5.750$, $P = 0.029$). There were no serious adverse events in both groups during the study period.

1 Kuntai capsule treatment of menopausal symptoms of traditional Chinese medicine theory and modern pharmacological research Chinese medicine called perimenopausal and early menopause for the " seven seven years " , at this time days Gui gradually, reproductive organs and breasts are gradually shrinking, will enter the old age The The reason is that the natural decay of the kidney qi, Tian Gui virtual, red Ren Yuan deficiency, is also kidney qi - days Gui - Chong Ren - uterine reproductive axis dysfunction. Postmenopausal women cognitive decline in one of the main pathogenesis of traditional Chinese medicine is the essence of blood loss, brain dystrophy, God disorders, and that " kidney bone marrow and on the brain " , and kidney relationship is particularly close.

Kuntai capsule group from the "Treatise on Miscellaneous Diseases" 303 in the Huanglian Ejiao Tang from the cut, there are nourishing blood, Qingxu heat, soothe the nerves Chufan effect. The main ingredients of 6 Chinese herbal medicines: Rehmannia sweet warm for nourishing yin, fill lean marrow to medicine, "Jing Yue Quan Shu · Materia Medica is" think " Yin blood deficiency all by the non-arable land can not ..... Yin And the spirit of scattered, non-cooked land of the defenders are not enough to gather " , there is the effect of nourishing the brain; scutellaria, Huang Lianqing heat dampness, Xiehuo detoxification; white peony convergence Yin, Ejiao Ziyin, Fuling Yi Xinpi, heart and kidney to soothe the nerves. Rehmannia and white peony, donkey-hide

gelatin, the benefits of essence and blood, acid and yin yin to acne, white peony and scutellaria, Huanglian phase Wu, sour bitterness to clear fire, Poria heart and spleen Ning heart, Tired of the spleen of the sex. All the indications of kidney yin deficiency, virtual fire endogenous to the post-menopausal syndrome.

The pharmacological mechanism of kuntai capsules is not clear at present, and it may be related to the phyto-estrogen-like effect of the ripening and white peony, and the modern pharmacological studies of Poria, Scutellaria and donkey-hide gelatin also suggest that the protective effect of monotherapy on the nervous system The Clinical studies have shown that kuntai capsules can increase the levels of E2 in postmenopausal women and shift the vaginal epithelium to the right [3] . Animal experiments show that Kuntai capsule can increase the ovarian volume of menopausal rats, the number of corpus luteum, uterine wet mass, can regulate endocrine and improve ovarian function [4] .

In vitro studies have shown that kontai capsules have the effect of protecting neurons and protect neurons from neurotoxicity of L -form glutamate, viral protein gp120 and beta amyloid peptide [5

] . Pharmacological studies have shown that CEE can significantly promote neuronal growth and resistance to oxidative damage [6] .
3. Effects of 2 Kuntai Capsule and CEE on Cognitive Function and Psychological Symptoms in Early Menopausal Women The results of this study show that MMSE scores are shown for 3 , 6 , 9 , and 12 months after early menopausal women, kuntai capsules or CEE treatment Compared with Gong Lili et al [7] , it suggested that Kuntai Capsule and CEE could maintain the normal cognitive function of early menopausal women, and the difference between the two drugs was Statistical significance. However, a systematic review of Cochrane [8] shows that in elderly postmenopausal women, hormone replacement therapy (CEE + medroxyprogesterone acetate) group cognitive function score lower than the placebo group, but the digital memory capacity has increased slightly. This study is not consistent with this systematic assessment may be due to the object of this study for early menopausal women (menopause time within 3 years), and the age of less than 60 years of age, the baseline MMSE score of 21 points or more, which Tierney et al [9] <A agreed i = 104> study population characteristics, the results also show estrogen group language learning function compared to placebo significantly improved; and the systematic review included literature, mostly aging women, 1 articles subjects aged > 60 years old the remaining 6 Pian were 65 or more years of age (where 1 Pian > 70 years of age, 1 Pian > 75 years old), some women have been cognitive impairment. Brinton [10] proposed the " estrogen-responsive healthy cell bias " hypothesis that estrogen protection effects only against the normal brain structure, once the brain degenerative changes, estrogen may have its opposite effect. Kupperman score, the psychological symptoms score showed that the two groups after treatment at each time point of the weight of the points before and after treatment showed a significant downward trend. There was no significant difference between the two intervention measures (ITT analysis $P = 0.117$, PPS analysis $P = 0$). 334), consistent with Zhang Jing et al [11] , suggesting that both drugs can improve the psychological status of early menopausal women, relieve insomnia, mood swings, depression and other psychological symptoms, and the results are similar, the results are more reproducible. There was no statistically significant difference between the two drugs and may be related to the smaller sample size. 3.3 CEE and Kuntai capsule in the course of the adverse reactions and the limitations of the study The two groups of the most common adverse reactions for the breast pain, but breast mammography were not found abnormalities, may be with the drug phytoestrogenic effect The impact on the breast. Irregular vaginal bleeding during treatment is also more common, hormone group was significantly higher than the Kuntai group (39.3% *vs* 11. 1%), randomized controlled studies have shown CEE

bleeding risk groups greater than Kuntai group [12], other randomized controlled studies have reported CEE treatment of peri-menopausal vaginal bleeding during the syndrome among women 25% - 66% range, vaginal bleeding may And estrogen increased, intimal breakthrough bleeding.

This study has some limitations. The long-term effects of the study drug on cognitive function are still unclear if the sample size is small, both Han women, the population is not representative, and the observation period is short, and the results are applicable to other race women. At the baseline of the two groups, the waist-to-hip ratio was higher in the hormone group than in the Kuntai group, and the waist-to-hip ratio was positively correlated with the testosterone and E2 ratio [13] , but there was no evidence that the waist-to-hip ratio and age-contact. As the subjects were not cognitive impairment, and for early menopausal women, may lead to sampling bias, for Kuntai capsule in the late menopausal cognitive function is normal, or postmenopausal women have cognitive impairment have the same The treatment effect remains to be further studied. The study found that kuntai capsule for early menopausal women's cognitive function has a protective effect, for insomnia, upset, doubts, anxiety and other psychiatric symptoms have a better therapeutic effect, the clinical effect as much as CEE , vaginal bleeding, breast swelling Pain and other adverse reactions than the incidence of CEE , better safety.

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