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SYSTEMATIC REVIEW

Comparison of the effect and safety of Kuntai capsule and hormone replacement therapy in patients with perimenopausal syndrome: a systematic review and Meta-analysis

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Abstract

OBJECTIVE: To assess the effectiveness and safety of Kuntai capsule and hormone replacement therapy in treatment of perimenopausal syndrome.

METHODS: Articles were retrieved from the databases Cochrane Database of Systematic Reviews, PubMed, Chinese National Knowledge Infrastructure, China Science and Technology Journal Database, and Wanfang Database. Only randomized controlled trials were included; 15 trials involving 1243 patients were identified from January 2005 to April 2015. A systemic review and Meta-analysis of publications was performed. The review was limited to randomized controlled trials that compared Kuntai capsule and hormone replacement therapy to treat perimenopausal syndrome for at least 3 months. The primary outcome assessed was the treatment efficacy at 3 months, including effective rate of Kupperman menopausal scores, Kupperman menopausal scores, and blood estradiol (E_2) or blood follicle stimulating hormone (FSH) levels. Other outcomes assessed were safety or adverse events, such as gastrointestinal complaints, breast distending pain, or vaginal bleeding.

RESULTS: Kupperman menopausal scores showed no significant difference in effective rate [odds ratio (*OR*): 1.05, 95% confidence intervals (*CI*): 0.71 to 1.55] and changes in FSH level [mean difference (*MD*): 2.14, 95% *CI*: − 2.36 to 6.65]. There was a significant statistical difference in Kupperman menopausal scores (*MD*: − 1.14, 95% *CI*: − 2.03 to − 0.25) and changes in E_2 level (*MD*: − 16.41, 95% *CI*: − 18.83 to − 13.69). There were fewer adverse events in the Kuntai capsule group than in the hormone replacement therapy group (*OR*: = 0.35, 95% *CI*: 0.25 to 0.48, $P < 0.01$).

CONCLUSION: Compared with hormone replacement therapy, Kuntai capsule can improve perimenopausal symptoms and blood E_2 levels, and reduce the incidence of adverse events.

Keywords: Hormone replacement therapy; Perimenopause; Postmenopause; Drug-related side effects and adverse reactions; Randomized controlled trial; Review

INTRODUCTION

Perimenopausal syndrome occurs during the perimenopausal period. It is characterized by a range of symptoms and signs; these are attributed to changes in sex hormones and seriously affect the patient's health and quality of life. [1]

Hormone replacement therapy (HRT) is often used to treat perimenopausal syndrome and it can effectively relieve symptoms and increase blood estrogen levels. However, many perimenopausal women are unable to take these kinds of drugs, owing to relative or absolute contraindications. In addition, long-term use of HRT can lead to adverse reactions, such as venous thrombosis and vascular diseases. [2]

Therefore, the identification of effective and safe alternative medications is an immediate priority. Traditional Chinese medical treatment may be an alternative therapy for patients with perimenopausal syndrome. Interest in Traditional Chinese Medicine (TCM) is increasing. One TCM medication is Kuntai capsule (KC), which contains six Chinese herbal medicines: Dihuang (*Radix Rehmanniae*), Huanglian (*Rhizoma Coptidis*), Baishao (*Radix Paeoniae Alba*), Ejiao (*Colla Corii Asini*), Huangqin (*Radix Scutellariae Baicalensis*), and Fuling (*Poria*). This formula is used to relieve a variety of clinical symptoms of early menopause and improve quality of life.[3]

In this Meta-analysis, our aim was to evaluate the effect and safety of KC, compared with HRT, in treating patients with perimenopausal syndrome.

METHODS

Search methods for identification of studies

The following databases were electronically searched: Cochrane Database of Systematic Reviews, PubMed, Chinese National Knowledge Infrastructure (CNKI), Chinese Science and Technology Journal Full-text Database (VIP), and the Wanfang database. Other related papers were also identified. Search terms included "Kuntai capsule," "Gengnianningxin capsule," "hormone replacement therapy," "perimenopausal syndrome," "climacteric syndrome," "menopausal syndrome," and "randomized controlled trial." The search included articles published from inception to April 2015. There were no language restrictions. The search strategy was as follows:

#1 Kuntai;
#2 Gengnianningxin capsule;
#3 Kuntai capsule;
#4 Gengnianningxin capsule;
#5 C21 steroids;
#6 #1 OR #2 OR #3 OR #4 OR #5;
#7 perimenopausal syndrome;
#8 peri-menopausal syndrome;
#9 climacteric syndrome;
#10 menopausal syndrome;
#11 #7 OR #8 OR #9 OR #10;
#12 randomized controlled trial;
#13 #6 AND #11 AND #12

Selection of studies

All citations were initially screened by two authors (Wang Lijun and Hao Yu) to select articles for full-text review. Any disagreement regarding the final selection of studies for inclusion was resolved by consensus with a third investigator (Du Xiaoqin). Studies were selected according to the following parameters:

Inclusion criteria

(a) Randomized controlled trial (RCT) design, diagnosis of perimenopausal syndrome; (b) treatment period ≥ 3 months; (c) reporting of the primary outcome.

Exclusion criteria

(a) Observational studies; (b) quasi-randomized or crossover studies; (c) case reports; (d) case series; (e) use of historical controls; (f) review articles.

Data extraction

Data were independently extracted from full-text articles by two authors. After extraction, data were reviewed and compared, with disagreements solved by consensus.

Definition of end points

(a) Kupperman menopausal scores (Table 1), odds ratios (or); (b) effective rate of Kupperman menopausal scores, or; (c) blood estradiol (e_2) or blood follicle stimulating hormone (FSH) levels; (d) incidence of adverse reactions (e.g., gastrointestinal complaints, breast distending pain, vaginal bleeding).

Assessment of methodological quality

All included studies were assessed using Jadad scoring (the Oxford quality scoring system) for clinical trials, which includes the reporting of randomization technique, presence and appropriateness of blinding, and description of dropouts and withdrawals.[4] In addition, we considered whether analysis was conducted according to the "intention-to-treat" principle (involving an a priori defined protocolization of interventions and a priori defined primary end points, as well as other end points).

Statistical analysis

Statistical calculations were performed using Cochrane Collaboration Review Manager (RevMan) 5.2 [Review Manager (RevMan) (Computer program). Version 5.2 Copenhagen: the Nordic Cochrane Centre, the Cochrane Collaboration]. Data from included studies were combined using a random-effects model expressed as an odds ratio (*OR*) with 95% confidence intervals (*CI*). For continuous data, the use of the mean difference (*MD*) is recommended when all trials used